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- (71) Applicant (for all designated States except US): **REPRO-GENESIS, INC.** [US/US]; 21 Erie Street, Cambridge, MA 02139 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **GENTILE, Frank, T.** [US/US]; 96 Flagg Hill Road, Boxborough, MA 01719 (US). **MELO, Antonio, P.** [US/US]; 24 Edith Road, Hudson, MA 01749 (US). **BIRKHEAD, James, R.** [US/US];

Apartment 2, 32 Colwell Avenue, Brighton, MA 02135 (US). **WEITZNER, Barry, D.** [US/US]; 3 MacLeod Lane, Acton, MA 01720 (US). **LOTITO, Mark, A.** [US/US]; 3 South Central Terrace, Wollston, MA 02170 (US).

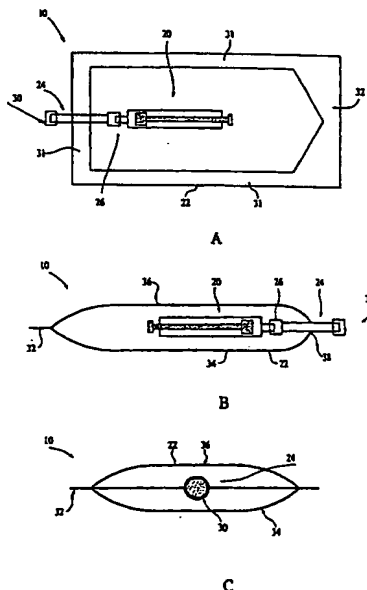
(74) Agents: **POSORSKE, Laurence, H. et al.**; Baker Botts, L.L.P., The Warner, 1299 Pennsylvania Avenue, N.W., Washington, DC 20004 (US).

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[Continued on next page]

(54) Title: **STERILE PACKAGING OF LIVE MATERIAL WITH IMPROVED STORAGE CHARACTERISTICS**



(57) Abstract: A storage package is disclosed. The storage package comprises an outer container; a second outer container completely enclosing the outer container; an access portal transiting the outer container; a cell containing compartment; a stabilizing bath compartment, wherein the stabilizing bath compartment is connected to the cell containing compartment through a semi-permeable barrier, wherein the semi-permeable barrier permits passage of molecular species but does not permit passage of living cells, and further wherein the semi-permeable barrier forms at least a portion of the barrier between the stabilizing bath compartment and the cell containing compartment, and wherein the outer container completely encloses the cell containing compartment and the stabilizing bath compartment; means for removing the second outer container; and means for removing the outer container.

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## STERILE PACKAGING OF LIVE MATERIAL WITH IMPROVED STORAGE CHARACTERISTICS

### 5 BACKGROUND OF THE INVENTION

#### 1. Field of the Invention

This invention relates generally to the field of storing and using living material therapeutically. More particularly, the invention relates to sterile packaging of live material with improved storage characteristics.

#### 10 2. Description of Related Art

In surgical procedures it is routinely necessary to provide sterile surgical instruments. Apparatuses and methods of sterilely introducing non-living material into a sterile field are known in the art, such as disclosed in United States Patent No. 4,065,816, to Sawyer, herein incorporated by reference. Sawyer discloses  
15 a method of packaging a prosthetic device for surgical use. The prosthetic device is packaged, sterilized in the package, and shipped to a sterile environment where the package is opened.

While these prior apparatus and methods have been successful with non-living material, they have not succeeded in translocating living material from  
20 off-site to a sterile field. Non-living material can be sterilized after being placed into a container, but living materials are adversely affected by the sterilization process and thus have to be treated differently.

Living material can be introduced in a sterile environment, although it is difficult. An example of sterile surgical use of living material is blood  
25 transfusion bags. Apparatuses and methods of sterilely using blood bag systems are known in the art, such as disclosed in United States Patent No. 3,942,529, to Waage, herein incorporated by reference. Waage discloses a package and method for storing blood. While blood bags are sterile before they are filled, after filled they are no longer sterile and extreme precaution has to be used once the bags are brought into a  
30 sterile environment.

Aseptic transfer is an alternative method for introducing living material into a sterile operating room. In this method, the living material is

aseptically packed in a vial. The outside of the vial is typically clean, but is not sterile. Therefore, to use the living material in the vial in the operating room, a non-sterile assistant has to open the vial and hold it for the sterile operator. The sterile operator would then draw the cells via a straw or other tube into a sterile syringe.

5 Only then can the living material be used in the sterile environment.

The current method of translocating living material into a sterile operating room is cumbersome and requires additional time and manpower to use the living material in a sterile manner. Therefore, a need has arisen for a new method and apparatus for aseptically packaging and dispensing live material that  
10 overcome the disadvantages and deficiencies of the prior art.

## SUMMARY OF THE INVENTION

In accordance with a principle aspect of the present invention, sterile packaging of live material with improved storage characteristics is disclosed. It is  
15 an object of this invention to allow living material to be aseptically introduced into a sterile field.

It is another object of this invention to provide an apparatus capable of sterilely storing and dispensing living material.

These and other objects are met by one or more of the following  
20 embodiments. In one embodiment, the invention provides a storage package comprising an outer container; a second outer container completely enclosing the outer container; an access portal transiting the outer container; a cell containing compartment; a stabilizing bath compartment, wherein the stabilizing bath compartment is connected to the cell containing compartment through a semi-  
25 permeable barrier, wherein the semi-permeable barrier permits passage of molecular species but does not permit passage of living cells, and further wherein the semi-permeable barrier forms at least a portion of the barrier between the stabilizing bath compartment and the cell containing compartment, and wherein the outer container completely encloses the cell containing compartment and the stabilizing bath  
30 compartment; means for removing the second outer container; and means for removing the outer container.

In another embodiment, the invention provides an inner container and an outer container completely enclosing the inner container. An access portal transits the outer container and is operative to introduce a labile fluid or solid from outside the outer container into the inner container without further breaching the integrity of the outer container. The access portal allows the labile fluid or solid to be put in the inner container without otherwise opening the outer container. The inner container is preferably detachably connected to the access portal. Additionally, the outer container is removable.

In another embodiment, the invention discloses a method for providing a fluid to a sterile field. The method involves sterilizing a storage package, the storage package comprising an outer container that completely encloses an inner container and a fluid-conducting conduit that transits the outer container, with the outer container being removable. The method further involves inserting a fluid from outside the outer container into the sterilized inner container through the fluid-conducting conduit such that the fluid does not breach the sterility of the outer container. The fluid typically comprises material which is labile to sterilization, such as desired living cells suspended therein and the fluid is usually substantially free of contaminant cells other than the desired living cells. This method provides for opening the outer container in proximity to a sterile field, and dispensing the fluid from the inner container. In accordance with this method, once the fluid is inserted into the storage package, the package is not subject to further gross sterilization.

In another embodiment, the invention discloses a method for storing a labile fluid or solid. The method involves sterilizing a storage package comprising an outer container that completely encloses an inner container where a sealable access portal transits the outer container. The outer container is removably sealed about the inner container. The method subsequently involves inserting a labile fluid or solid from outside the outer container into the inner container through the access portal, such that the labile fluid or solid does not breach the sterility of the outer container. The package and the labile fluid or solid are not subject to terminal sterilization subsequent to inserting the labile fluid or solid.

In another embodiment, the invention discloses a method for sterilely dispensing a labile fluid or solid. The method involves providing a storage package that comprises an outer container completely enclosing an inner container having a labile fluid or solid therein, with the inner container being detachably connected to an access portal that transits the outer container. The outer container is removable. The method also involves opening the outer container in proximity to a sterile environment and then dispensing the labile fluid or solid from the inner container.

In another embodiment, the invention discloses a storage package having an outer container; a labile material containing compartment; and a stabilizing bath compartment. The stabilizing bath compartment encloses at least a portion of the labile material containing compartment through a semi-permeable barrier. The semi-permeable barrier forms at least a portion of the barrier between the stabilizing bath compartment and the labile material containing compartment. The outer container completely encloses the stabilizing bath compartment. The storage apparatus may comprise a means for evacuating the labile material from said storage apparatus. Further, the storage may comprise a means for evacuating said stabilizing bath from said storage apparatus.

In another embodiment of the invention, a storage apparatus is disclosed having an outer container, a stabilizing bath and labile material compartment for containing stabilizing material and labile material. At least a portion of the stabilizing bath and labile material compartment is enclosed by the outer container. A means is provided for separating at least a portion of the stabilizing material from the labile material. The storage apparatus has a semi-permeable barrier enclosing at least a portion of the stabilizing bath and labile material compartment not enclosed by the outer container. The means for separating at least a portion of the stabilizing material from the labile material may be a plunger, connected to the semi-permeable barrier, that when depressed decreases a volume of the stabilizing bath and labile material compartment. Thus, forcing the stabilizing bath to filter through the semi-permeable barrier and separate from the labile material. Alternatively, the means for evacuating the stabilizing material is a syringe barrel enclosing a remaining portion of the stabilizing bath and labile material compartment not enclosed by the outer container. The syringe barrel has a

first and second end, wherein the first end is an open end connected to the stabilizing bath and labile material compartment allowing the barrel to communicate with the stabilizing bath and labile material compartment, and the second end has a movable plunger. The syringe barrel is rigidly connected to the semi-permeable barrier, both of which slidably engage inside the outer container to decrease a volume of the stabilizing bath and labile material compartment when the syringe barrel is depressed. Thus, forcing the stabilizing bath to filter through the semi-permeable barrier and separate from the labile material.

Use of the storage package of this invention permits a sterile operator to easily handle and use living material in a sterile environment while not risking contamination of the material, the sterile environment, or the sterile operator. In particular, the storage package of this invention is well suited for containing and presenting implants and cell-containing compositions used in tissue engineering.

Other objects and advantages of the invention are set forth in part in the description which follows, and in part, will be apparent from this description, or may be learned from the practice of the invention.

## BRIEF DESCRIPTION OF THE DRAWINGS

For a more complete understanding of the present invention, the objects and advantages thereof, reference is now made to the following descriptions taken in connection with the accompanying drawings in which:

Fig. 1A is a top perspective of a storage package according to one embodiment of the invention.

Fig. 1B is a side perspective of a storage package according to one embodiment of the invention.

Fig. 1C is an end perspective of a storage package according to one embodiment of the invention.

Fig. 2 illustrates a storage package with multiple inner containers according to another embodiment of the invention.

Fig. 3 illustrates a storage package with a thermoformed rigid tray outer container according to another embodiment of the invention.

**Fig. 4** illustrates a storage package with a flexible package outside an inner container according to another embodiment of the invention.

**Fig. 5** illustrates a storage package with multiple outer containers according to another embodiment of the invention.

5           **Fig. 6** is a perspective representation of a storage package according to another embodiment of the invention.

**Fig. 7** illustrates an example of the storage package of **Fig. 6** in use.

**Fig. 8** illustrates another example of the storage package of **Fig. 6** in use.

10           **Fig. 9** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 10** is perspective representation of a storage package according to another embodiment of the invention.

15           **Fig. 11** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 12** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 13** is perspective representation of a storage package according to another embodiment of the invention.

20           **Fig. 14** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 15** is perspective representation of a storage package according to another embodiment of the invention.

25           **Fig. 16** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 17A** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 17B** is perspective representation of a storage package according to another embodiment of the invention.

30           **Fig. 18** is perspective representation of a storage package according to another embodiment of the invention.



**Fig. 19** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 20** is perspective representation of a storage package according to another embodiment of the invention.

5       **Fig. 21** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 22** is perspective representation of a storage package according to another embodiment of the invention.

10       **Fig. 23** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 24** is perspective representation of a storage package according to another embodiment of the invention.

**Fig. 25** is perspective representation of a storage package according to another embodiment of the invention.

15       **Fig. 26** is perspective representation of a storage package according to another embodiment of the invention.

## DETAILED DESCRIPTION OF INVENTION

20       Typically, sterility is ensured for materials coming into a sterile environment, such as an operating room, by subjecting the materials to harsh conditions that kill any adventitious organisms. Such conditions include sterilizing heat, ionizing radiation, toxic gas, and the like. When the desired materials include living cells, or easily denatured proteins, nucleic acids, or other organic molecules, alternative procedures for handling these labile materials are needed.

25       The invention encompasses a method and apparatus for providing a living material to a sterile environment in a faster, easier, and improved manner. The apparatus includes a sterile inner container that is enclosed by an outer container which can be handled by a non-sterile operator or assistant without comprising the sterility of the inner container. To use the apparatus, the inner container is  
30       aseptically filled with a living material in an aseptic manner. The apparatus is transported to a non-sterile environment and handled by the non-sterile assistant. The non-sterile assistant can place the apparatus in proximity to a sterile field and

remove the outer container and a sterile operator can handle the sterile inner container without fear of breaching the sterility of the material, the operator, the field, or the inner container.

The invention is particularly beneficial for handling a labile fluid or solid, i.e., a material that undergoes detrimental chemical, physical, or biological changes or breakdown under sterilizing conditions. The labile fluid or solid of the various embodiments disclosed herein may be many things. For example, it may be cells, a cell-containing composition, blood, lymph, or an aqueous suspension containing a heat-denaturable material such as a therapeutic protein in an aqueous solution. The labile material may also be a solid, semi-solid, liquid, sheet (thin or thick), block, other three-dimensional structure, gel, or hydrogel such as particularly or completely hardened alginate. Preferably, the labile material will have cells distributed on the surface and/or throughout all or a portion of the material. The labile fluid or solid may also be cells by themselves, such as a block or sheet of living tissue.

Typically, the labile fluid or solid will be a cell-containing composition. In a preferred mode, the storage package of this invention is used to contain cell-containing compositions for implantation or tissue engineering as described in European Patent Publication Nos. 0299010 and 0469070; International Patent Publication No. WO 94/25080; or United States Patent No. 5,667,778, all herein incorporated by reference. Additionally, a material that could be used, especially in the embodiment depicted in Fig. 10, could be the composition depicted in United States Patent No. 5,567,612, herein incorporated by reference. Alternatively, the inner container may contain a fluid composed of living or non-living material. Typically, such material will be labile to the sterilization method used to sterilize the storage package. Further, the storage package disclosed in these embodiments can be used whether sterilized or non-sterilized.

To promote a more complete understanding of the embodiments of the present invention and its advantages, embodiments are discussed in more detail by referring to Figs. 1-26 of the drawings, like numerals being used for like and corresponding parts of the various drawings.

Referring particularly to Fig. 1A, there is shown a storage package according to a first embodiment of the invention. The storage package, indicated generally at 10, comprises an inner container 20 which is completely enclosed by an outer container 22. Outer container 22 has an end that contains a peelable element 32. The other three sides of outer container 22 are sealed at sealed edges 31. A fluid-conducting conduit 24 transits outer container 22. By transiting outer container 22, fluid-conducting conduit 24 allows something outside of outer container 22 to enter inside of outer container 22 without opening outer container 22. Fluid-conducting conduit 24 has an end 30 which is typically closed by a removable closure. For example, the closure at end 30 can include a luer connector, an opening, a cap, or a septum.

Fluid-conducting conduit 24 is detachably connected to inner container 20 at connection point 26. Because inner container 20 is detachably connected, inner container 20 can easily be removed from fluid-conducting conduit 24. The detachable connection may be, for example, a friction fit or luer connector. A labile fluid or cell-containing composition may be inserted into fluid-conducting conduit 24 at end 30 of fluid-conducting conduit 24 such that the labile fluid or cell-containing composition does not result in a breach of outer container 22 that would compromise sterility; the labile fluid or cell-containing composition originating from outside of outer container 22 ends up substantially inside of inner container 20, with little or preferably none of the cell-containing composition of fluid between the outside of inner container 20 and the inside of outer container 22. Thus, introduction of the labile fluid or cell-containing composition does not cause a breach of sterility inside of outer container 22. Further, the labile fluid or cell-containing composition is introduced into inner container 20 without otherwise opening outer container 22.

As shown in Fig. 1B, a side view of storage package 10 is depicted. Outer container 22 is formed of a lower layer 34, an upper layer 36, the upper and lower layers 34 and 36 being sealed at three sealed edges, and peelable element 32. Peelable element 32 can be removed to expose inner container 20. Peelable-element 32 can be formed of any material that facilitates easy removal. For example, peelable element 32 can be made of TYVEK® (100% high density polyethylene

sheet formed from flash-spun plexifilaments), paper, nylon, or foil. Peelable element 32 can also be a breathable or nonbreathable material. Nonbreathable peelable material is usually made from a plastic. Nonbreathable peelable element is typically two layers coated with an adhesive suitable for separation of the two layers of the peelable element to facilitate removal. Breathable peelable material can either be coated or non-coated. A non-coated peelable material typically generates a stronger seal, but is harder to open. Alternatively, peelable element 32 may be integrally connected to one or more of the upper and lower layers 34 and 36 such that opening peelable element 32 leads to peeling apart the upper and lower layers 34 and 36 at peelable sealed edges 31, shown in Figure 1A. Further, peelable element 32 may be a tear strip, as described in United States Patent No. 4,367,816, to Wilkes, herein incorporated by reference. Moreover, peelable element 32 may be a sealed edge that can be easily ripped or cut.

Referring again to **Fig. 1B**, fluid-conducting conduit 24 provides access to inner container 20 without breaching the seal of outer container 22 at 38. Preferably, the seal at 38 forms a strong seal around fluid-conducting conduit 24, to prevent leakage, such that access to inner container 20 is blocked from the outside of outer container 22, except for fluid-conducting conduit 24.

Fluid-conducting conduit 24 may be, for example, a septum port or a tube. In a typical embodiment, fluid-conducting conduit 24 is made from polyethylene. However, fluid-conducting conduit 24 can be made of any material that can be sealed to outer container 22. For example, such materials are, but not limited to, polyethylene terephthalate glycol, polyvinyl chloride, polystyrene, polyethylene terephthalate, polyethylene, polyester (such as MYLAR®), SCLAIR® (linear low density polyethylene), TYVEK®, paper, nylon, or foil. In an alternative embodiment, fluid-conducting conduit 24 may be substituted by an access portal to facilitate the introduction of a labile fluid or solid comprising larger particles into inner container 20.

In **Fig. 1C**, an end view of storage package 10 is depicted. Lower layer 34 and upper layer 36 are shown to connect at sealing element 32. End 30 of fluid-conducting conduit 24 is depicted, where a labile fluid or cell-containing composition would be introduced. A luer fitting could be fitted onto end 30 to

facilitate easy connection to a syringe or some other device for introducing the labile fluid or cell-containing composition. Alternatively, end 30 could be a septum for inserting a needle into fluid-conducting conduit 24 or an access conduit that can allow the labile fluid or cell-containing composition to be introduced aseptically.

5                   End 30 of fluid-conducting conduit 24 is ordinarily sealed to prevent leakage and maintain the sterility of inner container 20. Means for sealing end 30 of fluid-conducting conduit 24 can include any method of sealing end 30 such that a barrier exists between fluid-conducting conduit 24 and the environment of outside outer container 22. For example, sealing means may include a heat seal of end 30 to  
10                   completely seal end 30, a clasp that clamps shut end 30, a cap for end 30, a fluid seal that seals end 30, or a valve to seal end 30.

                  In the embodiment depicted in Figs. 1A to 1C, inner container 20 is a syringe; however, inner container 20 can be any containing device. Inner container 20 may be made of any suitable rigid material, such as metal, glass, polypropylene,  
15                   polycarbonate, or polyethylene. Preferably, inner container 20 will be constructed to facilitate dispensing the labile fluid or cell-containing composition on demand. For example, inner container 20 can be a bag made of any flexible material, and the contents dispensed by squeezing the bag. Any of the components of storage package 10 can be substituted for any of the like components described with respect  
20                   to the other embodiments disclosed herein.

                  In Fig. 2, a storage package 110 containing multiple inner containers is depicted. In addition to inner container 120, a second inner container 140 is also completely enclosed by outer container 122. Inner container 120 has an end 142 and inner container 140 has an end 144. Ends 142 and 144 can be alternatively  
25                   connected to end 126 of fluid-conducting conduit 124. Additional inner containers can be introduced into outer container 122. Further, additional elements can be enclosed within outer container 122, such as needles, cannulae, dispensing valves, bottles, wash fluid, fittings such as a stopcock, connectors, or delivery catheters and mechanisms. Additionally, any other elements that would assist in the delivery of  
30                   the labile fluid or cell-containing composition, or could easily be assembled and fit within outer container 122, could also be enclosed within outer container 122. In particular, elements that are to be used in the sterile field in conjunction with

administration of the labile fluid or cell-containing composition may be enclosed within outer container 122, where they are maintained in sterile condition and readily available at the time the labile fluid or cell-containing composition is dispensed.

5           A tray 146 can be used as a frame inside of outer container 122 to hold inner containers 120 and 140. Tray 146 is molded to the shape of inner container 120 and 140 to hold inner containers 120 and 140. Use of tray 146 not only keeps inner containers 120 and 140 from being jostled during transit, but also provides an easy method of removing inner containers 120 and 140. For example,  
10       tray 146 may be bendably distortable so that when outer container 122 is removed, tray 146 can be contorted to force out inner containers 120 and 140 successively or simultaneously without directly touching inner containers 120 and 140. While tray 146, as depicted, can maintain one or two inner containers, the structure of tray 146 can be altered to maintain any number of inner containers. Tray 146 can be made of  
15       any rigid material, for example polyethylene terephthalate glycol, polyvinyl chloride, polystyrene, polyethylene terephthalate, or polyethylene, and preferably tray 146 is elastically distortable. Additionally, all of the components of storage package 110 can be substituted for any of the like components described with respect to the other embodiments.

20           In Fig. 3, a storage package 210 is depicted including an outer container 250 comprising a thermoformed tray 252 and a peelable element 232. Thermoformed tray 252 provides a sturdy outer container to protect inner container 220 and maintain the sterility of inner container 220. Peelable element 232 can be easily removed to expose inner container 220. To remove peelable element 232, a  
25       user needs only to grasp thermoformed tray 252 and pull outward on peelable element 232. This will separate peelable element 232 from thermoformed tray 252, exposing inner container 220. Additionally, thermoformed tray 252 can be shaped to hold inner container 220, with a tray analogous to tray 146. Thermoformed tray 252 can be made of any sturdy material, including but not limited to polyethylene  
30       terephthalate glycol, polyvinyl chloride, polystyrene, polyethylene terephthalate, or polyethylene. Peelable element 232 can be formed of any material that facilitates easy removal. For example, peelable element 232 may be made of TYVEK®,

paper, nylon, or foil. Alternatively, thermoformed tray 252 may be substituted by a sheet of flexible material, mentioned herein, sealed to peelable element 232 to form outer container 250. Variations on these structures using combinations of flexible and rigid material will be readily apparent to those skilled in the art, and are within the contemplation of this invention (see, e.g., Fig. 4).

A hermetic seal 238 forms a strong seal around fluid-conducting conduit 224. End 230 allows entry of material from outside outer container 250 to inside of inner container 220 via fluid-conducting conduit 224. For example, end 230 can be a check valve or stopcock. Additionally, each of the components of storage package 210 can be substituted for any of the like components described with respect to the other embodiments.

As shown in Fig. 4, a storage package 310 includes an optional flexible package 362 surrounding an inner container 364. Inner container 364 is analogous to outer containers 22, 122, and 250 of Figs. 1-3 and surrounds inner container 320. Inner container 364 has a built-in rigid member 366 supporting a fluid-conducting conduit 324. Flexible package 362 provides a flexible container that protects inner container 364 and inner container 320 and helps maintains the sterility of inner container 364 and inner container 320. Typically, storage package 310 is sterilized. Then, in a sterile environment, flexible package 362 can be removed and inner container 320 can be filled with a labile fluid or cell-containing composition. This leaves the sterile inner container 320 filled with the labile fluid or cell-containing composition surrounded by inner container 364.

Inner container 364 covers inner container 320 and holds rigid member 366. Flexible package 362 and inner container 364 can be made of any flexible material, for example, polyethylene, polyester (such as MYLAR®), SCLAIR®, TYVEK®, paper, nylon, or foil. Inner container 364 and flexible package 362 can each include a peelable element to facilitate easy opening. Rigid member 366 can be made of any rigid material mentioned herein. Rigid member 366 assists in forming a strong seal around fluid-conducting conduit 324. End 330 allows entry of material from outside inner container 364 via fluid-conducting conduit 324. End 330 can be covered with an end cap 390 or other capping or sealing mechanism.

As shown, inner container 320 has an optional connector 396 that couples septum 392 to inner container 320. A user can manipulate inner container 320, with septum 392 at its end, from outside of inner container 364 to fit into needle housing 398 so that needle 394 penetrates septum 392. After removing flexible package 362, a labile fluid or cell-containing composition may be inserted through fluid-conducting conduit 324 into inner container 320. After filling inner container 320, septum 392 can be removed from needle 394, separating inner container 320 from fluid conducting conduit 324. Inner container 320 could also be entirely disassembled from connectors, such that a user could assemble inner container 320 and connectors as needed. Additionally, multiple connectors and fittings, preferably having male/female luer connectors, could be used to facilitate connection between inner container 320 and fluid-conducting conduit 324. Moreover, each of the components of storage package 310 can be substituted for any of the like components described with respect to the other embodiments.

Further, storage package 310 could be surrounded by a rigid exterior tray, such as tray 146 depicted in Fig. 2, such that after removing flexible package 362 and after filling inner container 320, inner container 364 enclosing inner container 320 could be held into place by the rigid tray. Alternatively, storage package 310, before flexible package 362 has been removed, could be inserted into a rigid exterior tray. Using a rigid exterior tray could assist in the shipping, mechanical manipulation, or protecting of inner container 364 and inner container 320.

In Fig. 5, a storage package 410 with multiple outer containers is depicted. A first outer container 470 is similar to outer container 250. First outer container 470 includes a thermoformed tray 472 and a peelable element 474, that are similar to thermoformed tray 252 and peelable element 232, respectively. A second outer container 480 completely encloses first outer container 470. Second outer container 480 includes a thermoformed tray 482 and a peelable element 484, that are similar to thermoformed tray 252 and peelable element 232, respectively. However, fluid-conducting conduit 424 extends through the multiple outer containers to the outside of second outer container 480, allowing a labile fluid or cell-containing composition to be introduced from outside of second outer container 480 into inner



container 420. Having multiple outer containers provides additional protection and sterility. Storage package 410 can have any number of outer containers as long as fluid-conducting conduit 424 extends through the outermost outer container. In fact, any of the components of storage package 410 can be substituted for any of the like components described with respect to the other embodiments.

In Fig. 6 storage package 510 according to another embodiment of the present invention is depicted. Outer container 522 completely encloses inner container 520, and tray 546 holds inner container 520 in place. While storage package 510 is similar to storage package 10, a significant difference between the two embodiments is that outer container 522 has opening 556 that provides controlled access to the interior of outer container 522. Typically opening 556 will be sealed before and after filling of inner container 520 with a labile fluid or cell-containing composition. End 542 of inner container 520 can be lined up with opening 556 for the filling operation. End 542 can include an opening, a septum, a luer connector, or a stopper. For example, end 542 can be made of cork, rubber, or plastic. As depicted, fluid-conducting conduit 524 is a hollow needle connected to a syringe 590, which is part of the filling apparatus. Syringe 590 can be filled with a suitable fluid which may be a cell-containing composition or may contain other material that is labile to sterilization. Fluid-conducting conduit 524 is detachably connected to inner container 520 during the filling operation, for needle 524 passes through or into end 542 of inner container 520 and is removable after filling inner container 520. Additionally, any of the components of storage package 510 can be substituted for any of the like components described with respect to the other embodiments.

After inserting the labile fluid or cell-containing composition into inner container 520, needle 524 can be removed. To seal outer container 522, opening 556 can be sealed with sealing device 558, as shown in Fig. 7. For example, sealing device 558 can be a cap, a luer connector, a valve, a fluid valve, a clamp that shuts opening 556, or a heat seal such that opening 556 is heat sealed shut.

To maintain sterility of storage package 510 after sterilization and before filling inner container 520, an outer sterile barrier 564 can be enclosed

entirely around outer container 522 as shown in Fig. 8. Outer sterile barrier 564 can be, for example, made of any material that can maintain the sterility of outer container 522 and inner container 520. For example, polyethylene, low density polyethylene, polyester (such as MYLAR®), SCLAIR®, TYVEK®, paper, nylon, or foil can be used. Additionally, outer sterile barrier 564 can be rigid or flexible, thus, for example, polyethylene terephthalate glycol, polyvinyl chloride, polystyrene, or polyethylene terephthalate, could also be used. Typically, package 510 would be sterilized with barrier 564 in place, and barrier 564 would be removed immediately prior to filling inner container 520 with material that is labile to sterilization.

In operation, the storage package of all the embodiments function similarly. The storage package is sterilized by a known sterilization means. Typically, the storage package is filled aseptically using a sterile filling apparatus, preferably involving a biosafety cabinet. To fill the inner container, a labile fluid or solid is inserted from outside of the outer container into the inner container through an access portal, which may be a fluid-conducting conduit. The access portal allows the labile fluid or solid to be introduced into the inner container without otherwise opening the outer container. Additionally, the labile fluid or solid does not breach the sterility inside of the outer container. Thus, the labile fluid or solid does not substantially enter the area between the outside of the inner container and the inside of the outer container. The labile fluid or solid may or may not be sterile. Where the labile solid or fluid contains a desired population of living cells, but otherwise is substantially free of contaminant cells other than those living cells, the only non-sterile material in the sterile storage package would be those desired living cells. If, however, the labile solid or fluid does not contain living cells, but rather non-living labile material, then everything in the storage package may be sterile.

After inserting the desired labile fluid or solid into the inner container, any excess labile fluid or solid left in the access portal or fluid-conducting conduit can be pushed into the inner container by using some means to remove the excess labile fluid or solid. Any means for purging the access portal or fluid-conducting conduit of excess labile fluid or solid is acceptable. For example, the excess material can be pushed using a rod, by forcefully blowing air into the access

portal or fluid-conducting conduit, or by tapping the access portal or fluid-conducting conduit. The end of the access portal or fluid-conducting conduit may then be closed. Any sealing means may be used as long as a good seal is created that keeps the inner container sterile. The storage package may then be translocated  
5 to a sterile field, such as an operating room.

The storage package, once filled with the labile fluid or solid, is not further subjected to terminal sterilization. Terminal sterilization would kill everything living in the storage package. Because the labile fluid or solid preferably contains living material or other materials labile under sterilizing conditions,  
10 terminal sterilization would adversely affect the labile fluid or solid. Therefore, gross sterilization of the package is only performed prior to insertion of the labile fluid or solid.

A non-sterile operator or assistant may then take the storage package and bring it into the operating room or adjacent to a sterile field. The non-sterile  
15 assistant can remove the outer container of the storage package. To remove the outer package, the non-sterile operator might simply peel off the peelable element of the outer container, tear or rip open the outer container, or cut the outer container. Once the outer container has been opened, a sterile operator can grasp the inner container (or one of them if there are several) and disconnect it from the access  
20 portal or fluid-conducting conduit, if it is attached. Alternatively, if the inner containers are contained by a tray, the non-sterile assistant can bend the tray such that an inner container pops out into the sterile field or the sterile operator's hand. Alternatively still, the non-sterile assistant can dump the inner containers out of the outer container, once the outer container has been opened. Alternatively still, if the  
25 inner container is a container, the sterile operator can grasp the container. Alternatively still, if using a live material, such as a skin sample, the non-sterile assistant can open the inner container and let the sterile operator grasp the sample. Alternatively still, if using a sample that has solidified in the inner container to a desired shape, the sterile operator could open the inner container and remove the  
30 sample. Typically the solidified sample will be a cell-containing composition or material, such as a preformed implant; however, it is within the contemplation of this invention that the preformed implant contain material labile to sterilizing

conditions, such as a therapeutic protein, but no cells. The outer container according to this invention can be removed or opened such that inner container is not contaminated and the inner container is not exposed to any non-sterile surface.

Once the sterile operator has the inner container, the sterile operator  
5 can dispense the labile fluid or solid. If the inner container is a syringe, the syringe plunger can be pushed to dispense the contents. If the inner container is a container, the inner container can be squeezed to release the desired labile fluid or solid.

To more completely describe the method of the present invention, the method will be further described with relation to the particular embodiment depicted  
10 in Figs. 1A-1C. However, the method as described below could be readily adapted for operation with the storage package of any of the embodiments disclosed herein. End 30 of fluid-conducting conduit 24 reversibly is sealed. Means to seal end 30 include, for example, heat sealing the end, a cap, a fluid valve, a valve, or clamping shut end 30. Storage package 10, with end 30 sealed, is then sterilized to kill  
15 substantially all contaminating organisms in storage package 10. Preferably, residual contamination will be at or below the level acceptable under good manufacturing practices for medical devices. Storage package 10 could be sterilized with any suitable method, for example, by steam, ethylene oxide, gamma irradiation, electron beam irradiation, or with ultraviolet light.

20 After being subjected to sterilization by a suitable means, inner container 20 is filled aseptically. In one example, storage package 10 is transported to a biosafety cabinet, such as a class 100 sterilization hood. Once inside of the biosafety cabinet, the removable seal on end 30 of fluid-conducting conduit 24 is removed. The labile fluid or cell-containing composition is then inserted into inner  
25 container 20 of storage package 10. The labile fluid or cell-containing composition may be inserted by any one of numerous methods. In one embodiment, a sterile filling syringe, with a luer lock is connected to end 30 of fluid-conducting conduit 24. This filling syringe can be connected manually or mechanically, such that sterility in the interior of the biosafety cabinet is not breached. The filling syringe is  
30 then emptied into fluid-conducting conduit 24 and the labile fluid or cell-containing composition is forced into inner container 20. After filling inner container 20, the filling syringe is removed. Optimally, any excess labile fluid or cell-containing

composition left in fluid-conducting conduit 24 can be pushed into inner container 20 by using any means for purging fluid-conducting conduit 24 of excess fluid, for example by using a rod to push the excess fluid into inner container 20, by forcefully blowing air into fluid-conducting conduit 24, or by tapping fluid-conducting conduit 24. After the labile fluid or cell-containing composition has been inserted into inner container 20, end 30 of fluid-conducting conduit 24 is then sealed again with any of the above methods. End 30 can even be permanently sealed with heat. At this point, storage package 10 is not subsequently subjected to terminal sterilization that would affect the labile fluid or cell-containing composition.

Terminal sterilization is a final sterilization that substantially kills all living things prior to shipment of a sterile product. Accordingly, terminal sterilization would adversely affect the labile fluid or cell-containing composition after inner container 20 of storage package 10 has been filled. However, so long as the labile fluid or cell-containing composition is substantially free of contaminants other than the desired cells, and inner container 20 is sterile prior to inserting the labile fluid or cell-containing composition, once the labile fluid or cell-containing composition is inserted aseptically, inner container 20 will be substantially free of living cells except for the desired cells that are completely enclosed in inner container 20. Of course, if the fluid only contained nonliving material, storage package 10 could be subject to terminal sterilization after the nonliving material is inserted into inner container 20, unless the non-living material was labile under the conditions of the terminal sterilization.

Storage package 10 is then typically transported to the point of use, which may be an operating room with a sterile environment. At this point, the inside of outer container 22 and the outside of inner container 20 will be sterile (i.e., substantially free of contaminating organisms). Additionally, the inside of inner container 20 will be sterile, except for the desired labile fluid or cell-containing composition. A non-sterile assistant in the operation room can peel open outer container 22, exposing inner container 20 without contaminating it. A sterile operator can then grasp inner container 20 and twist inner container 20 free from the luer connector. Alternatively, if tray 46 was used, the non-sterile assistant could remove outer container 22 and push inner container 20 free from the tray 46 by

indirect pressure without contaminating the outside of inner container 20, allowing inner container 20 to fall either into the sterile environment or the sterile operator's hand. Alternatively, if inner container 20 was no longer attached to fluid-conducting conduit 24, outer container 22 could be removed by the non-sterile assistant without touching inner container 20 directly, and the sterile operator could either grasp inner container 20 or let it fall out of outer container 22 into the sterile field.

After removing inner container 20, the sterile operator can use inner container 20 to dispense the labile fluid or cell-containing composition. For example, if inner container 20 is a syringe, the labile fluid or cell-containing composition can be dispensed through the syringe. Alternatively, if inner container 20 is a flexible bag, inner container 20 can be depressed to squeeze or squirt out the labile fluid or cell-containing composition.

It will be noted that everything contained within outer container 22 and translocated to the sterile environment will typically be in sterilized and in clean condition, previously untouched until grasped by the sterile operator. Further, if inner container 20 is a syringe or a bag, then only the exterior of inner container 20 would be touched by the sterile operator. The needle, cell-containing composition, or fluid would typically be entirely untouched by any operator. Thus, the labile fluid or cell-containing composition is aseptically introduced to the sterile field or patient.

Methods for using other embodiments of this invention for manipulation of labile fluids or solids in sterile environments will be analogous to the method described in detail for use of the embodiment of Fig. 1 with a cell-containing composition.

As shown in Fig. 9, a storage package 610 according to another embodiment of the present invention is depicted. An outer container 622 completely encloses an inner container 620, and a tray 646 holds inner container 620 in place. While storage package 610 is similar to storage package 510, the significant difference between the two embodiments is that outer container 622 has a flap 664. Flap 664 includes an access portal 624. Access portal 624 can be aligned with an end 642 of inner container 620. Access portal 624 allows a labile fluid or solid, to enter from outside of outer container 622 and into inner container 620. Additionally,

any or all of the components of storage package 610 can be substituted for any of the like components described with respect to the other embodiments.

In operation, storage package 610 may operate as follows. End 642 of inner container 620 is not originally connected to access portal 624, but rather  
5 inner container 620 is free floating within outer container 622. Storage package 610 is sterilized and then translocated to a filling station, for example a biosafety cabinet. While in the biosafety cabinet, end 642 can be connected to access portal 624. End 642 can be connected using any known connecting means. Preferably, outer container 622 is a flexible material which may be manipulated to align end 642 with  
10 access portal 624. After sterilizing storage package 610 and connecting end 642 to access portal 624, a labile fluid or solid is inserted from outside of outer container 622 to inside of inner container 620. After inserting the labile fluid or solid, end 642 is disconnected from access portal 624 and access portal 624 is closed. Access portal 624 can be sealed by heating outer container at the area marked 668, or fusing  
15 closed access portal 624. Alternatively, it can be sealed with any method that provides a barrier to contamination of the sterility of inside outer container 622, for example, with a clamp, by melting the ends of access portal 624 in some other manner, with a cap, a valve, a fluid valve, or stopper. Accordingly, inner container 620 is free floating within the completely sealed outer container 622. Alternatively,  
20 the tip of end 642 can be fused or heated shut along with access portal 624. In that case, inner container 620 would be connected to the completely sealed outer container 622. Regardless, access portal 624 is removed and is no longer part of storage package 610.

Storage package 610 is then translocated to a location adjacent to a  
25 sterile environment or field. Once in or near the sterile environment or field, a non-sterile assistant can remove outer container 622. One such method could be to cut, tear, or rip along dotted line 676, removing flap portion 668. However, outer container 622 can be removed in any conventional manner as long as the non-sterile assistant does not come into substantial contact with inner container 620. After  
30 removing outer container 622, a sterile operator can grasp inner container 620, if inner container 620 has a graspable portion that is easily grasped, or can allow inner container 620 to fall out from outer container 622. If inner container 620 is still

connected to outer container 622, inner container 620 can be sterilely removed by any suitable means. The labile fluid or solid can then be sterilely dispensed.

As shown in Fig. 10, a storage package 710 according to another embodiment of the present invention is depicted. Storage package 710 is well suited to handle solid materials, including tissues such as a living skin sample, but would also function well with any other labile fluid or cell-containing material, for example in the form of sheets (thin or thick), blocks, or other three dimensional structures. Typically the solid material will be a cell-containing material, such as a preformed tissue implant; however, it is within the contemplation of this invention that the solid be a matrix containing material labile to sterilizing conditions, such as a therapeutic protein, but no cells. Inner container 720 may resemble a container for storage and distribution of a skin wound dressing container disclosed in Tubo *et al.*, U.S. Patent No. 5,040,677, incorporated herein by reference, except that access portal 724 extends into inner container 720. In a typical example, inner container 720 includes thermoformed tray 772 and an peelable element 774. Outer container 722 completely encloses inner container 720, and access portal 724 also transits outer container 722. Alternatively, access portal 724 can be a joining point of inner container 720 and outer container 722, as depicted in Figure 10. Outer container 722 can alternatively be made of a flexible material, as previously disclosed. Additionally, any or all of the components of storage package 710, can be substituted for any of the like components described with respect to the other embodiments.

After sterilizing storage package 710, a sample 790 could be sterilely inserted through access portal 724 in a sterile hood or other environment suited for aseptic filing, and into inner container 720. After inserting sample 790, access portal 724 may be sealed by any sealable means, including the previously mentioned means. After sealing, storage package 710 may be translocated to a sterile field. Once package 710 is in proximity to the sterile field, a non-sterile assistant can remove outer container 722 by any of the fore-mentioned means, including separating peelable element 784. Then a sterile operator can remove sterile peelable element 774 and remove sample 790.



Alternatively, inner container 720 could be a molded shape. A cell-containing composition or other labile fluid could be inserted into inner container 720 such that once inside, the cell-containing composition or other labile fluid solidifies into the shape of the molded inner container 720. To use, outer container 5 722 and inner container 720 could be removed, exposing the molded sample to manipulation by the sterile operator.

Alternatively, a seedable substrate could be placed in inner container 720, either before or after the storage package 710 has been sterilized. If the substrate is placed in inner container 720 before the storage package 710 is 10 sterilized, the storage package 710 should be sterilized before living cells are introduced to the inner container 720. Cells or some other cell-containing composition may then be sterilely introduced to the inner container, as described above, to seed the substrate with cells or other cell-containing composition. When the cells, that have now been seeded by the substrate, are to be removed, they may 15 be removed as described above.

**Fig. 11** shows an embodiment of a storage package according to this invention. As shown in **Fig. 11**, a cell containing compartment 807 is enclosed by a stabilizing bath compartment 809; stabilizing bath compartment 809 is enclosed by an outer sterile container 804; and outer sterile container 804 is optionally enclosed 20 by an second outer container 801. Cell containing compartment 807 and stabilizing bath compartment 809 comprise releasable container 832. In a preferred embodiment, releasable container 832 is freely removable from the storage package upon opening outer sterile container 804. Molded conduit 803 is integrally incorporated into outer sterile container 804. Channel 812 transits molded conduit 25 803. Preferably, channel 812 integrally includes fluid transporter 805. Fluid transporter 805 can be inserted into cell containing compartment 807 through access portal 810 of stabilizing bath compartment 809. By transiting molded conduit 803, and access portal 810 fluid transporter 805 allows access from outside of outer sterile container 804 to the inside of cell compartment 807, without opening outer 30 sterile container 804. Ordinarily, the storage package is treated to make it sterile and then a fluid composition containing living cells is introduced into cell containing compartment 807 through fluid transporter 805. As shown in **Fig. 11**, cell

containing compartment 807 retains labile material, such as cell containing composition 811. Cell containing compartment 807 provides liquid/liquid contact of cell stabilization material 808 and cell containing composition 811, while preventing release of cell containing composition 811 into cell stabilizing material 808.

5 Typically, the walls of cell containing compartment 807 are constructed to facilitate the exchange of certain components between cell stabilization material 808 and cell containing composition 811. The pore size of the walls of cell containing compartment 807 permits transfer of desired components, but does not permit transfer of cells. Preferably, the pore size of the walls of cell compartment 807 is

10 0.1 to 0.4 microns. The walls of cell containing compartment 807 may be made of any suitable micro-porous material. Further, the walls of cell containing compartment 807 may be made of any suitable porous material, such as, Gortex, PTFE, polycarbonate, polyacrylonitrile, porous polyethylene, PDMS, PET, nylon, a co-polymer of polyacrylonitrile and vinyl chloride, or any suitable porous silicon-

15 based material. The walls of cell containing compartment 807 may be flexible or rigid. Alternatively, a suitable matrix, which entraps labile material, particularly cells, and permits transfer of desired components, but does not permit transfer of cells, may be used in place of the cell containing compartment.

The shape of cell containing compartment 807 is designed to

20 maximize the exchange of desired components between cell stabilization material 808 and cell containing composition 811. Maximizing the surface area to volume ratio of cell containing compartment 807, for example, with a flatly-shaped cell containing compartment 807, maximizes desired component exchange. Cell containing compartment 807 is fixed to access portal 810 with a suitable attachment

25 mechanism, such as an adhesive. Cell containing compartment 807 is enclosed by stabilizing bath compartment 809. Preferably, the surface area of the wall of cell compartment 807 is maximized, commensurate with the desired volume ratio between cell stabilization material 8 and cell containing composition 811.

Cell stabilization material 808 comprises soluble components to

30 support and stabilize cell containing composition 811 contained inside of cell containing compartment 807. Cell stabilization material 808 is contained within stabilizing bath compartment 809, which includes access portal 810, and bounded by

cell containing compartment 807. Preferably, cell stabilization material 808 substantially surrounds cell containing compartment 807 for maximum solute transfer. Cell stabilization material 808 comprises a solution capable of providing support and stabilization to cell containing composition 811. For example, the support may be a medium which includes nutrients for cells in cell containing composition 811, such as cell culture nutrient media, M199, RPMI, or DMEM, or may be any isotonic solution, such as isotonic saline. Cell stabilization material 808 may also contain serum, or can be serum-free, may also contain buffer, or can be buffer-free. The most common material for use as a cell stabilization material 808 is cell culture media, but the skilled worker will recognize that references to media below are only exemplary of any solution that contains solutes which can serve to stabilize cells for storage.

The volume of cell stabilization medium 808 is typically sufficient to provide that cell containing composition 811 does not experience significant changes in environment over time, for example, due to changes in cell containing composition 811 resulting from cellular metabolism. Generally, maintaining a suitable cell environment requires a larger volume of cell stabilization medium 808 than the volume of cell containing composition 811. Preferably, the volume ratio of cell stabilization medium 808 to cell containing composition 811 is in the range from 5:1 to 200:1. If longer storage times are desired, a higher ratio may be used.

The cell stabilizing medium 808 may be introduced into the stabilizing bath compartment 809 in any of a variety of ways. For example, if the cell stabilizing medium 808 is stable to the sterilization procedure (e.g., heat sterilization for isotonic saline or gamma irradiation for cell culture medium), the cell stabilizing medium 808 may be sealed into in the stabilizing bath compartment 809 before the package is sterilized. This procedure obviates the need for a separate port for introduction of the cell stabilizing medium. Alternatively, as shown in Fig. 12, cell stabilizing medium 908 may be inserted into the stabilizing bath compartment 909 after sterilization of the package via an access port 920 in the stabilizing bath compartment 909. Cell stabilizing medium 908 may be filter sterilized by, for example, passing the cell stabilizing medium 908 through a 0.2 micron filter before introducing it into the stabilizing bath compartment 909.

Referring again to Fig. 11, after filling the cell containing compartment 807 with cells 811, the cells 811 in contact with the cell stabilizing medium 808 may be stored under suitable storage conditions. Typically, cells will be stored at temperatures between 1°C and 40°C, and the gaseous atmosphere surrounding the storage system may include 5% CO<sub>2</sub>, depending on whether the walls of the storage system are gas permeable and whether CO<sub>2</sub> atmospheres are beneficial for the particular cell type. Cell storage times are contemplated ranging from hours to days or weeks. In a preferred embodiment, the cells are stored for 14 days while a formal USP sterility test (which involves a 14 day incubation period), may be performed to confirm sterility of the package.

The volume and type of cell stabilizing medium 808 may vary are depending on the desired shelf life for the cells. Variations in the storage temperature, cell density, and cell type will also affect shelf life of the stored cells. The skilled worker will optimize all of these parameters to optimize the packaging for the desired shelf life. For example, increasing the medium-to-cell ratio will tend to prolong shelf life at the expense of increasing the weight of the package and possibly degrading its handling characteristics. Alternatively, for some embodiments of the storage system of this invention, aged medium may be withdrawn and replaced with fresh medium periodically to lengthen shelf life of the cells without increasing the weight of the package. Similarly, shelf life for most cell types can be extended by reducing storage temperature, permitting lower medium-to-cell ratios and lower package weight for comparable storage times.

Stabilizing bath compartment 809 retains cell stabilization medium 808 in a compact and manipulable form. Stabilizing bath compartment 809 retains cell stabilization medium 808 inside its walls, allowing the exchange of desired components between cell stabilization medium 808 and cell containing composition 811. Stabilizing bath compartment 809, containing access portal 810, substantially encloses cell stabilization medium 808 and cell containing compartment 807. Stabilizing bath compartment 809 is heat-sealed or otherwise connected to access portal 810. Stabilizing bath compartment 809 is made of a material suitable for retaining cell stabilization medium 808 and suitable for connection to access portal 810. Stabilizing bath compartment 809 is preferably made of polyethylene if access

portal 810 is also made of polyethylene to facilitate heat sealing of these two components. Stabilizing bath compartment 809 may also be made of any flexible material, for example, polyester (such as MYLAR® (E.I. duPont de Nemours and Company)), SCLAIR®, TYVEK® (E.I. duPont de Nemours and Company), paper, or foil. Access portal 810 is made of a material suitable for connection to stabilizing bath compartment 809, such as polyethylene if stabilizing bath compartment 809 is also made of polyethylene. The materials capable of contacting cell containing solution 811 or cell stabilization medium 808, including stabilizing bath compartment 809, access portal 810, cell compartment 807, injection site 806, and fluid transporter 805, are typically made of a biocompatible material.

Access portal 810 allows fluid transporter 805 to insert cell containing composition 811 into cell containing compartment 807 from outside of outer sterile container 804. Access portal 810 is connected to cell containing compartment 807, and to stabilizing bath compartment 809. Preferably, access portal 810 is connected to injection site 806. Injection site 806 may be fixed to access portal 810 and to stabilizing bath compartment 809. Injection site 806 maintains the sterility of cell containing composition 811, by preventing matter other than materials which can penetrate injection site 806, such as fluid transporter 805 and its contents, from passing through injection site 806. Injection site 806 is made of material that may be resealed after a penetrating object is removed. For example, injection site 806 can be made of rubber and polycarbonate. Injection site 806 may also be made of a biocompatible material suitable for connection to stabilizing bath compartment 809, such as polyethylene, if stabilizing bath compartment 809 is also made of polyethylene.

Channel 812 transits molded conduit 803. Channel 812 is capable of being capped, for example by deadender plug 802. Preferably, channel 812 integrally includes fluid transporter 805. Fluid transporter 805 is capable of introducing cell containing composition 811 from outside of outer sterile container 804 to the inside of cell containing compartment 807, without opening outer sterile container 804. Fluid transporter 805 is capable of transiting molded conduit 803, access portal 810, and injection site 806. Fluid transporter 805 is any object capable of allowing fluid that is inserted into one end of fluid transporter 805 to exit from an

opposite end of fluid transporter 805. In one embodiment, fluid transporter 805 may be a KLEEN-NEEDLE® (Tri-State Hospital Supply Corporation) described in references U.S. Patent No. 5,088,984, to Fields *et al.* and U.S. Patent No. 5,098,395 to Fields *et al.*, incorporated herein by reference, or alternatively, may be adapted  
5 from the KLEEN-NEEDLE® design by optionally eliminating one or more structural elements. Deadender plug 802 may cap the fluid transporter 805. Alternatively, fluid transporter 5 may be completely removable and deadender plug 802 would cap molded conduit 3.

Outer sterile container 804 prevents contamination of cell containing  
10 composition 811. Outer sterile container 804 substantially encloses cell containing compartment 807 and stabilizing bath compartment 809. Outer sterile container 804 is enclosed by and connected to molded conduit 803 to block undesired mass transfer inside outer sterile container 804 from outside of outer sterile container 804. Outer sterile container 804 and molded conduit 803 are made of materials suitable  
15 for connection to one another, such as polyethylene. Non-limiting examples of suitable fixture processes include heat sealing and use of a suitable adhesive. Outer sterile container 804 may also be made of any flexible material, for example, polyester (such as MYLAR®), SCLAIR®, TYVEK®, paper, or foil.

Outer sterile container 804 can be handled by a non-sterile operator  
20 or assistant without comprising the sterility of stabilizing bath compartment 809. Outer sterile container 804 can be made of a material suitable to maintain the sterility of stabilizing bath compartment 809, such as polyethylene or TYVEK®. Outer sterile container 804 may also be made of any flexible material, for example, polyester (such as MYLAR®), SCLAIR®, TYVEK®, paper, or foil. Outer sterile  
25 container 804 has an end that contains a peelable element 825. Peelable element 825 can be removed to expose stabilizing bath compartment 809. Peelable-element 825 can be formed of any material that facilitates easy removal. For example, peelable element 825 can be made of TYVEK®, paper, nylon, or foil. Peelable element 825 can also be a breathable or nonbreathable material. Nonbreathable peelable material  
30 is usually made from a plastic. Nonbreathable peelable element is typically two layers coated with an adhesive suitable for separation of the two layers of the peelable element to facilitate removal. Breathable peelable material can either be

coated or non-coated. A non-coated peelable material typically generates a stronger seal, but is harder to open. Alternatively, peelable element 825 may be integrally connected to one or more of the upper and lower layers such that opening peelable element 825 leads to peeling apart the upper and lower layers. Further, peelable element 825 may be a tear strip, as described in United States Patent No. 4,367,816, to Wilkes, herein incorporated by reference. Moreover, peelable element 825 may be a sealed edge that can be easily ripped or cut. Upon opening sterile container 804 with peelable element 825, releasable container can be readily removed from the storage package.

10                    Preferably, sterile container 804 is handled by a non-sterile operator and opened in such a way that releasable container 832 is provided to a sterile operator without compromising the sterility of the sterile operator or releasable container 832. Optionally, second outer container 801 completely encloses outer sterile container 804 during sterilization of the storage package, and may contain a peelable element or tear strip as previously mentioned. To permit easy opening of  
15                    second outer container 801 for filing cell containing compartment 807.

                    When using a cell storage system that includes an integral media bath for stabilizing the stored cells, the procedure for dispensing the cells is similar to the process used for other cell storage and transport systems of this invention. The  
20                    following description of the process of dispensing the releasable container, using Fig. 11 as an example, applies to all figures. Typically, both the cell containing compartment 807 and the stabilizing bath compartment 809, together comprising releasable container 832, will be released from the package into the sterile field. Where the cell containing compartment 807 is a syringe barrel, cells may be  
25                    dispensed manually by pushing the plunger, and suitable cannulae may be attached to the syringe. Where the cell containing compartment 807 is a flexible tube, squeezing the tube will manually extrude the contents. Cell containing composition 811 contained inside of cell containing compartment 807 can be transferred to another item, for example, a syringe. For example, cells from the cell containing  
30                    tube may be extruded into a syringe barrel or taken up into a syringe, and subsequently injected into the desired location.

As shown in Fig. 12, a storage package 910 including access portal 920, which is connected to stabilizing bath compartment 909, but is not connected to cell containing compartment 907, is depicted. Access portal 920 allows the introduction of cell stabilization medium 908 into stabilizing bath compartment 909.

5 This embodiment allows for introduction of cell stabilization medium 908, initially and optionally periodically, for periodic insertion of cell stabilization material 908, for example, to increase storage time, or to promote new cell growth of cell containing composition 911.

10 In one embodiment of a storage package with more than one access portal, as depicted in Fig. 12, access portal 920 allows fluid transporter 905 to insert cell stabilization medium 908 into stabilizing bath compartment 909 from outside of outer sterile container 904, without opening outer sterile container 904. Fluid transporter 905, which transits channel 912 is a preferred method of introducing cell stabilization medium 908 to the inside of stabilizing bath compartment 909. Access  
15 portal 920 is connected to stabilizing bath compartment 909. Access portal 920 is made of a biocompatible material suitable for connection to stabilizing bath compartment 909, such as polyethylene if stabilizing bath compartment 909 is also made of polyethylene. Preferably, access portal 920 contains injection site 916. Injection site 916 may be fixed to access portal 920 and to stabilizing bath  
20 compartment 909. Injection site 906 maintains the sterility of cell stabilization medium 908, by preventing matter other than materials which can penetrate injection site 916, such as fluid transporter 905 and its contents, from passing through injection site 916. Injection site 916 is made of material as previously mentioned. Cell containing compartment 907 and stabilizing bath compartment 909  
25 comprise releasable container 932. Outer sterile container 904 completely encloses stabilizing bath compartment 909 and may contain a peelable element or tear strip as previously mentioned. Optionally, second outer container 901 completely encloses outer sterile container 904 and may contain a peelable element or tear strip as previously mentioned.

30 In another embodiment of a storage package with more than one access portal, as depicted in Fig. 12, in addition to channel 912, alternatively, an additional channel may also transits molded conduit 903. The additional channel



may be capped, for example by a deadender plug. Preferably, the additional channel is integrally include an additional fluid transporter. The additional fluid transporter 915 introduces cell stabilization material 908 from outside of outer sterile container 904 to the inside of stabilizing bath compartment 909, without opening outer sterile container 904. The additional fluid transporter also transits molded conduit 903, 5 outer sterile container 904, and access portal 920. If injection site 916 is connected to access portal 920, as preferred, the additional fluid transporter transits injection site 916. The additional fluid transporter is any object capable of allowing fluid that is inserted into one end, to exit from an opposite end. In one embodiment, the 10 additional fluid transporter may be a KLEEN-NEEDLE® as previously mentioned.

As shown in Fig. 13, a storage package 1010 according to another embodiment of the present invention is depicted. Storage package 1010 is well suited to handle solid materials, such as a solid tissue sample or a polymeric matrix containing cells or an effective amount of dissociated human cells and a polymeric 15 matrix suitable for example, to form or to augment breast tissue, but would also function well with any other cell containing material or fluid. A typical cell-containing solid within this embodiment of the present invention is described in U.S. Patent No. 5,716,404, to Vacanti *et al.*, "A method for augmentation or reconstruction of breast tissue" incorporated herein by reference. In a typical 20 example, stabilizing bath compartment 1039 encloses cell containing solid 1037 and cell stabilization medium 1038. Thus, stabilizing bath compartment 1039 corresponds to the releasable container of Figs. 11 and 12. Cell containing solid 1037 is in liquid/liquid contact with cell stabilization medium 1038, permitting diffusion of medium components to cells 1041. Optionally, cell containing solid 25 1037 may be surrounded by a semi permeable membrane analogous to the cell containing compartment wall of Figs. 11 and 12. Stabilizing bath compartment 1039 is typically made of material as previously mentioned for analogous components of other embodiments. Cell containing solid 1037 may be surrounded by porous walls comprised as previously mentioned. Cell stabilization medium 30 1038 is bound by stabilizing bath compartment 1039. Preferably, cell stabilization material 1038 substantially surrounds cell containing solid 1037 for maximum exchange of desired components between cell stabilization material 1038 and cells

1041. Cell stabilization material 1038 comprises a stabilization medium as previously mentioned. The volume ratio of cell stabilization material 1038 to cell containing solid 1037 should be a ratio as previously mentioned for other embodiments. Outer sterile container 1034 completely encloses stabilizing bath compartment 1039. Second outer container 1031 completely encloses outer sterile container 1034. Outer sterile container 1034 may comprise peelable element 1032 as previously mentioned. Access portal 1040 transits second outer container 1031. Alternatively, access portal 1040 can be a joining point of outer sterile container 1034 and second outer container 1031 as depicted in Fig. 13. Second outer container 1031 and outer sterile container 1034 may be made of a flexible material as previously disclosed. Additionally, any or all of the components of storage package 1010, can be substituted for any of the like components described with respect to the other embodiments.

After sterilizing storage package 1010, a cell containing solid 1037 could be sterilely inserted through an access portal 1040 in a sterilization hood or other environment suited for aseptic filling and into outer sterile container 1034. After inserting cell containing solid 1037, access portal 1040 may be sealed by any sealable means, including the previously mentioned means. Typically cell containing solid 1037 will be placed in stabilizing bath compartment 1039 at or before the time it is placed inside inner sterile compartment 1034.

Optionally, a fluid transporter may transit access port 1040 and a channel through stabilizing bath compartment 1039 to conduct media exchange during storage. Alternatively, a fluid transporter may transit second outer container 1031 and outer sterile container 1034 by portals other than access portal 1040 to conduct media exchange during storage.

One embodiment of the releasable container of Figs 11 and 12 is depicted in Fig. 14. Jacketed syringe system 1100 may be enclosed inside of the outer sterile container of a storage system, such as the ones embodied in Fig. 11 and Fig. 12. Again referring to Fig. 14, syringe system 1100 jacketed is placed inside the outer sterile container of Figs. 11 and 12 to allow storage of cell containing composition 1111 and, upon opening of the outer sterile container is released to allow a sterile operator to inject cell containing composition 1111 into a desired

location. Jacketed syringe system 1100 comprises a syringe 1120 substantially enclosed by jacket 1130. Cell stabilization material 1108 is bound by syringe 1120 and the jacket 1130. Preferably, the surface area of syringe 1120 that is in contact with cell stabilization medium 1108 is maximized. Alternatively, to facilitate an operator looking into syringe 1120, the surface area of syringe 1120 that is in contact with cell stabilization medium 1108 may be less than maximized. Syringe 1120 is capable of retaining cell containing composition 1111. The walls of syringe 1120 are made of porous material as previously mentioned to allow desired component exchange between cell containing composition 1111 and cell stabilization material 1108.

In the embodiment of a releasable container depicted in Fig. 15, plunger reservoir system 1200 may be enclosed inside of the outer sterile container of a storage system, such as the ones embodied in Fig. 10, 11, 12 and 13. Again referring to Fig. 15, plunger reservoir system 1200 allows storage of cell containing composition 1211 and allows a sterile operator to inject cell containing composition 1211 into a desired location. Plunger reservoir system 1200 comprises barrel 1201 and plunger shaft 1202. Plunger shaft 1202 is typically removable from barrel 1201. Barrel 1201 is capable of containing retaining cell containing composition 1211. Plunger shaft 1202 is capable of retaining cell stabilization medium 1208. Plunger shaft 1202 may comprise porous wall 1204. Porous wall 1204 is preferably connected to the end of plunger shaft 1204 opposite plunger handle 1206. Porous wall 1204 is made of porous material as previously mentioned to allow desired component exchange between cell containing composition 1211 and cell stabilization medium 1208. Plunger barrel 1201, plunger handle 1206, and plunger shaft 1202, with the exception of the porous wall, are comprised of a suitable impermeable rigid material.

If plunger shaft 1202 is manufactured to include porous wall 1204 and cell stabilizing medium 1208 in place, plunger reservoir system 1200 may be placed in a storage package according to any embodiment of this invention and sterilized. After sterilization, cell containing composition 1211 is introduced as described herein. Alternatively, syringe barrel 1201 and plunger shaft 1202 maybe sterilized separately and the syringe loaded by placing cell containing composition

1211 into barrel 1201, followed by porous wall 1204, cell stabilization material 1208, and plunger shaft 1202. Thus assembled plunger reservoir system 1200 may be placed in the storage package of this invention, e.g., by inserting through access portal 724 of Fig. 10 or access port 1040 of Fig. 13, for storage.

5 In the embodiment depicted in Fig. 16, media packet system comprising syringe 1300 may be enclosed inside of the outer sterile container of a storage system, such as those embodied in Fig. 10-13 and Fig. 13. Again referring to Fig. 16, media packet system comprising syringe 1300 allows storage of cell containing composition 1311 and allows a sterile operator to inject cell containing  
10 composition 1311 into a desired location. Media packet system comprising syringe 1300 comprises a syringe barrel 1301 capable of retaining cell containing composition 1311 and capable of retaining media packets 1303. Media packets 1303 are capable of retaining cell stabilization material 1308. The walls of media packets 1303 are made of porous material as previously mentioned to allow desired  
15 component exchange between cell containing composition 1311 and cell stabilization material 1308. The cross-sectional area of each media packet 1303 at every angle is preferably greater than the cross sectional area of syringe orifice 1307, allowing cell containing composition 1311 to exit syringe orifice 1307, but not allowing media packets 1303 to exit syringe orifice 1307 when syringe plunger 1309  
20 is depressed. Media packets 1303 are loaded into syringe barrel 1301 ahead of syringe plunger 1309; subsequently, syringe plunger 1309 is inserted into syringe barrel 1301 for a limited distance. Syringe barrel 1301 and syringe plunger are made of rigid, impermeable solids, molded into a desired shape.

If the cell stabilization medium is stable to sterilization, assembled  
25 media packet system syringe 1300 may be sterilized in place inside the outer sterile container and cell containing composition 1311 introduced after sterilization as described herein for other embodiments. Alternatively, presterilized syringe barrel 1301 may be filled with a mixture of cell containing composition 1311 and media packets 1303 before presterilized syringe plunger 1309 is inserted, and thus  
30 assembled media packet system syringe 1300 may be inserted through access portal 724 of Fig. 10 or access portal 1040 of Fig. 13 for storage.

In the embodiment depicted in Fig. 17A, storage package system comprising syringe 1405 may be enclosed within sterile container 1430. Syringe 1405 comprises plunger 1409, porous sleeve 1418, and container 1412. Sterile container 1430 comprises conduit 1424 extending outward, end 1425 connected to  
5 conduit 1424, and housing 1470 extending inward. Housing 1470 comprises needle 1420. Syringe 1405 communicates with end 1425 of sterile container 1430 via needle 1420.

Syringe 1405 may be used to store labile material, such as a cell containing composition, in a sterilized manner as follows. External syringe 1460  
10 holding cell containing composition 1410 may be connected and used to inject composition 1410 into end 1425. During injection, cell containing composition travels through conduit 1424 and needle 1420 into porous sleeve 1418 of syringe 1405. Cell stabilizing medium 1440 may be placed within syringe 1405 between container 1412 and porous sleeve 1418 prior to injection of labile material. Porous  
15 sleeve 1418, made of porous material as described in previous embodiments, allows cell stabilizing medium 1440 to contact cell containing composition 1410. However, as shown in Fig. 17B, when plunger 1409 is activated, cell containing composition 1410 is expelled through tip 1480 of syringe 1405 because cell stabilizing medium 1440, and not the cells, will pass through porous sleeve 1418.

The above embodiment is applicable to cell containing compositions that are solid products as well as fluid type products.. Alternatively, a gellable composition containing cells may be introduced into porous sleeve 1418 in liquid  
20 forma and allowed to gel in-situ. In the case of a cell containing composition having a solid form, a sealable transfer tube may be used in place of needle 1420 to insert the solid into the porous sleeve.

In the embodiment depicted in Fig. 18, porous sleeve 1418 and plunger 1409 may be removed from syringe 1405. The drawing on the left shows syringe 1405 after removal from sterile container 1430 as embodied in Fig. 17. Container 1412 and cell stabilizing material 1440 may be removed from syringe  
30 1405, thereby leaving porous sleeve 1418 with cell containing composition 1450, as shown in the center drawing of Fig. 18. Porous sleeve 1418, plunger 1409, and cell

containing composition 1450 may be placed in empty syringe 1405, as shown in the right drawing.

In another embodiment depicted in **Fig. 19**, syringe 1600 comprises plunger 1610 and valve 1630. Syringe 1600 may hold cell containing composition 1620, in the form of a gel rod, and cell stabilizing material 1640. Valve 1630 is provided to drain cell stabilizing material 1640. Valve 1630 may have a porous filter so that only cell stabilizing material exits valve 1630 and not the labile material.

In another embodiment depicted in **Fig. 20**, cell containing composition 1720 is extracted from first container 1760 into second container 1750. As shown in the left drawing, containers 1760 and 1750 are connected along an axis. Container 1760 comprises porous sleeve 1770 separating cell containing composition 1720 from cell stabilizing material 1740, but, allowing liquid/liquid contact between the two. Plunger 1710 of container 1750 is pulled upward to extract cell containing composition 1720 into second container 1750. Because porous sleeve 1770 allows cell stabilizing material 1740, but not cell composition 1720, to pass through porous sleeve 1770, only cell containing composition 1720 flows into second container 1750, as shown in the right drawing.

Referring to **Fig. 21**, a method and system for transferring cell containing composition 1860 and cell stabilizing material 1870 into container 1820 with sterile container 1830, according to another embodiment of the invention is shown. The top drawing of Fig. 21 depicts connector 1840 for connecting product container 1820, within sterile container 1830, to syringe 1825. Syringe 1825 is connected to syringe 1815 via link 1850. Plungers 1810 and 1805 are used respectively with syringes 1825 and 1815. Plunger 1810 extends through container 1820 and sterile container 1830. Cell containing material 1860 in syringe 1815 is drawn into container 1820 by pulling plunger 1810 away from syringe 1825. After cell containing material is drawn into container 1820, syringe 1815 may be replaced with a syringe to inject cell stabilizing material 1870 into container 1820. Upon container 1820 receiving both cell stabilizing material 1870 and cell containing material 1860, syringes 1815 and 1825 are disconnected from sterile container 1830 and sterile container 1830 is cut and sealed.

In another embodiment depicted in **Fig. 22**, the shape of labile gel 1920 is such that when syringe 1900 is inverted, the gel will not block the syringe opening so that the cell stabilizing material will flow out.

5 In another embodiment depicted in **Fig. 23**, plunger 2040 has a filter tip to allow cell stabilizing material to pass through and be stored in chamber 2030 when the plunger is activated.

In another embodiment depicted in **Fig. 24**, labile gel rod 2120 is formed on the end of plunger 2130 and placed inside container 2100 holding cell stabilizing material 2110. Labile gel rod 2120 may be removed from container 2100  
10 by lifting plunger 2130 and placed into empty container 2140, as shown from left to right in the figure.

**Fig. 25** depicts a storage apparatus according to another embodiment of the invention. Storage apparatus 2200 comprises syringe barrel 2208, porous sleeve 2220, plungers 2230 and 2240. Porous sleeve 2220 is enclosed by container  
15 2205. Porous sleeve 2220 allows labile gel rod 2250 inside container 2205 to be in contact with cell stabilizing material 2210, as shown in step 1. Plunger 2230 has a length that when fully depressed, pushes labile gel rod into syringe barrel 2208, as shown in step 2. Plunger 2240 has a length that when fully depressed, pushes labile gel rod out of syringe barrel 2208 and away from storage apparatus 2200, as shown  
20 in step 3.

-----Another embodiment of the invention is depicted in **Fig. 26**. Storage  
apparatus 2300 comprises syringe 2305 with plungers 2310 and 2320. Plunger 2310  
has filtered tip 2340 so that when activated, cell stabilizing material 2325 filters out  
of syringe 2305 while labile gel 2315 flows into the chamber of plunger 2310.  
25 Plunger 2320 may be activated to expel the labile gel from the syringe.

While use of the storage aseptic package of this invention has been described in terms of an operating room containing a sterile field, where the package is opened and used by a non-sterile assistant and sterile operator, respectively, those skilled in the art will recognize that the apparatus and methods for its use are easily  
30 adapted to other environments with similar requirements, including a sterile manufacturing facility or a sterile field in an outpatient clinic. The non-sterile assistant may be substituted by mechanical means of opening the second outer

container, or even by one hand of the sterile operator while preventing contamination of the other hand which remains in the sterile field.

### Example

The effects of storage on cell viability were tested in a model system using chondrocytes dispersed in alginate hydrogel. Chondrocytes were obtained by cartilage biopsy taken from a normal human volunteer. Chondrocytes were isolated from the biopsy material using a collagenase digestion process as described in Atala, et al. (1994), *J. Urol.*, **152**:641 and Klagsbrun (1979), "Large-scale Preparation of Chondrocytes," *Meth. Enzymol.*, **58**:560. Isolated chondrocytes were expanded in T-flask and roller bottle cultures over a 4-8 week period.

Test samples were prepared by suspending cells from the expanded chondrocyte population in M199 and combining them with 2.2% Pronova UP MVP sodium alginate. Hydrogel aliquots were formed by combining 2.75 mL of cell-alginate suspension with 0.25 mL of M199 containing 6.0 mg of solid  $\text{CaSO}_4$ . The final cell concentration in the hydrogel was  $30 \times 10^6$  cells/mL.

The survival of cells in these hydrogel aliquots was tested under various storage conditions, and compared to normal cell storage under low cell density conditions (i.e., control cells stored at  $3.8 \times 10^4$  cells/mL). The hydrogel aliquots were stored under sterile conditions with or without a surrounding bath of cell culture medium M199 (30 mL of medium per 3 mL of cell-containing hydrogel) at either room temperature or  $4^\circ\text{C}$ . The gaseous atmosphere for the room temperature storage chamber containing the sample with a surrounding bath of M199 medium contained 5%  $\text{CO}_2$ .

The viability of the cells stored under the various conditions was measured at 24 and 48 hours by removing a portion of the hydrogel and dissolving it (using chelating agents) and then determining viability of the cells in the resulting solution by trypan blue exclusion. The results are shown in Table 1. As shown, chondrocytes in a hydrogel aliquot stored at room temperature with a bath of culture medium surrounding the hydrogel will retain cell viability as well as cells stored under normal cell storage conditions (i.e., low cell density or high medium-to-cell ratio). Cell viability decreased faster under all other conditions. This indicates that, while the cell concentration (i.e., cell-to-medium ratio) is an important aspect



affecting cell viability upon storage, cells may be stabilized to storage without diluting the cell density in a cell containing hydrogel by providing a bath of medium surrounding the hydrogel (effectively reducing the cell-to-medium ratio without actual dilution).

5                   While the present invention has been described in terms of numerous different embodiments, it will be apparent to the skilled artisan that the description of one embodiment may be consulted for guidance in design or operation of another embodiment, particularly with regard to construction materials and sizes. Thus, the particular description of any one embodiment is not limiting upon the scope of the  
10 invention, which is only limited by the appended claims.

**CLAIMS:**

We claim:

1. A storage package comprising:  
an outer container;  
5 an access portal transiting said outer container;  
a cell containing compartment;  
a stabilizing bath compartment, wherein said stabilizing bath compartment is connected to said cell containing compartment through a semi-permeable barrier, wherein said semi-permeable barrier permits passage of  
10 molecular species but does not permit passage of living cells, and further wherein said semi-permeable barrier forms at least a portion of said barrier between said stabilizing bath compartment and said cell containing compartment, and wherein said outer container completely encloses said cell containing compartment and said stabilizing bath compartment; and  
15 means for removing said outer container.
2. The storage package of claim 1, wherein a labile fluid or solid is in said cell containing compartment.
3. The storage package of claim 1, further comprising a second outer container completely enclosing said outer container and means for removing said  
20 second outer container.
4. A storage package comprising:  
an outer container;  
a labile material containing compartment; and  
a stabilizing bath compartment, wherein said stabilizing bath  
25 compartment is enclosing at least a portion of said labile material containing compartment through a semi-permeable barrier, wherein said semi-permeable barrier permits passage of molecular species but does not permit passage of labile material, and further wherein said semi-permeable barrier forms at least a portion of said barrier between said stabilizing bath compartment and said labile material  
30 containing compartment, and wherein said outer container completely encloses said stabilizing bath compartment.

5. The storage apparatus of claim 4, further comprising means for evacuating said labile material from said storage apparatus.

6. The storage apparatus of claim 5, wherein said labile material containing compartment is a syringe having a plunger, and said means for  
5 evacuating said labile material is said plunger.

7. The storage apparatus of claim 5, wherein said labile material containing compartment is a syringe having a first and second plunger;

said means for evacuating said labile material is said first and second  
plunger; said first plunger has a length that when said first  
10 plunger is fully depressed, said labile material is transported from a portion of said  
labile material containing compartment enclosed by said stabilizing material  
compartment to an other portion of said labile material containing compartment not  
enclosed by said stabilizing material compartment; and

said second plunger has a length that when fully depressed, said  
15 labile material is evacuated from said other portion of said labile material containing  
compartment not enclosed by said stabilizing material compartment to outside said  
storage apparatus.

8. The storage apparatus of claim 5, wherein said labile material is  
evacuated from said storage apparatus without evacuating said stabilizing material.

20 9. The storage apparatus of claim 5, wherein said labile material  
containing compartment is removable from said storage apparatus.

10. The storage apparatus of claim 4, further comprising means for  
evacuating said stabilizing bath from said storage apparatus.

11. The storage apparatus of claim 10, wherein said stabilizing material is  
25 evacuated from said storage apparatus without evacuating said labile material.

12. The storage apparatus of claim 4, wherein said labile material is a cell  
containing composition.

13. A storage apparatus comprising:  
an outer container,  
30 a stabilizing bath and labile material compartment for containing  
stabilizing material and labile material, wherein at least a portion of said stabilizing  
bath and labile material compartment is enclosed by said outer container,

means for separating at least a portion of said stabilizing material from said labile material.

14. The storage apparatus of claim 13, further comprising  
a semi-permeable barrier enclosing at least a portion of said  
5 stabilizing bath and labile material compartment not enclosed by said outer container, wherein said semi-permeable barrier permits passage of molecular species but does not permit passage of labile materials.

15. The storage apparatus of claim 14, wherein said means for separating at least a portion of said stabilizing material from said labile material is a plunger, connected to said semi-permeable barrier, that when depressed decreases a volume  
10 of said stabilizing bath and labile material compartment, thereby forcing said stabilizing bath to filter through said semi-permeable barrier and separate from said labile material.

16. The storage apparatus of claim 14, wherein said means for evacuating  
15 said stabilizing material comprises:

a syringe barrel enclosing a remaining portion of said stabilizing bath and labile material compartment not enclosed by said outer container, wherein said syringe barrel has a first and second end, said first end is an open end connected to said stabilizing bath and labile material compartment allowing said barrel to  
20 communicate with said stabilizing bath and labile material compartment, and said second end has a movable plunger; said syringe barrel is rigidly connected to said semi-permeable barrier; said syringe barrel rigidly connected to said semi-permeable barrier slidably engages inside said outer container to decrease a volume of said stabilizing bath and labile material compartment when said syringe barrel is  
25 depressed, thereby forcing said stabilizing bath to filter through said semi-permeable barrier and separate from said labile material.

17. The storage apparatus of claim 16, wherein said plunger has a length that when said plunger is fully depressed and said syringe barrel is fully depressed, at least a portion of said labile material is evacuated from said storage apparatus.

30 18. The storage apparatus of claim 17, wherein said labile material is a cell containing composition.

19. Method for providing a fluid to a sterile field comprising:

sterilizing a storage package comprising a second outer container that completely encloses an outer container, a fluid-conducting conduit that transits said outer container, said outer container being removable and said second outer container being removable, wherein said outer container completely encloses a cell  
5 containing compartment;

inserting a fluid from outside said second outer container into said cell containing container through said fluid-conducting conduit such that said fluid does not breach sterility of inside of said second outer container, said fluid comprising desired living cells suspended therein, said fluid further being  
10 substantially free of contaminant cells other than said desired living cells, wherein said fluid is in contact with a cell stabilizing medium, wherein said cell stabilizing medium is in a stabilizing bath compartment separated from said fluid by a semi-permeable barrier, wherein said semi-permeable barrier permits passage of molecular species between said fluid and said cell stabilizing medium, and wherein  
15 said outer container completely encloses said stabilizing bath compartment;

removing said second outer container;

opening said outer container in proximity to a sterile field; and

dispensing said fluid from said cell containing container into said sterile field, wherein subsequent to said step of inserting said fluid into said cell  
20 containing container, said storage package is not subject to terminal sterilization.

20. Method for storing a labile fluid or solid comprising:

sterilizing a storage package comprising an outer container, an access portal that transits said outer container, said outer container being removable;

inserting a labile fluid or solid from outside said outer container into  
25 said outer container through said access portal such that said labile fluid or solid does not breach sterility of inside of said outer container, wherein said labile fluid or solid is not subject to sterilization subsequent to said step of inserting said labile fluid or solid; and

storing said storage package, such that said labile fluid or solid is  
30 provided with a cell stabilizing medium through a semi-permeable barrier, wherein said semi-permeable barrier is in contact with a stabilizing bath compartment,

wherein said stabilizing bath compartment contains said cell stabilizing medium, wherein said outer container completely encloses said stabilizing bath compartment.

21. The method of claim 20, wherein said labile fluid or solid is inserted into a cell containing compartment.

- 5           22. Method for sterilely dispensing a labile fluid or solid comprising:  
            providing a storage package comprising an outer container, wherein  
said outer container completely encloses a stabilizing bath compartment and a cell  
containing compartment, wherein a labile fluid or solid is in said cell containing  
compartment, an access portal that transits said outer container, said outer container  
10   being removable;

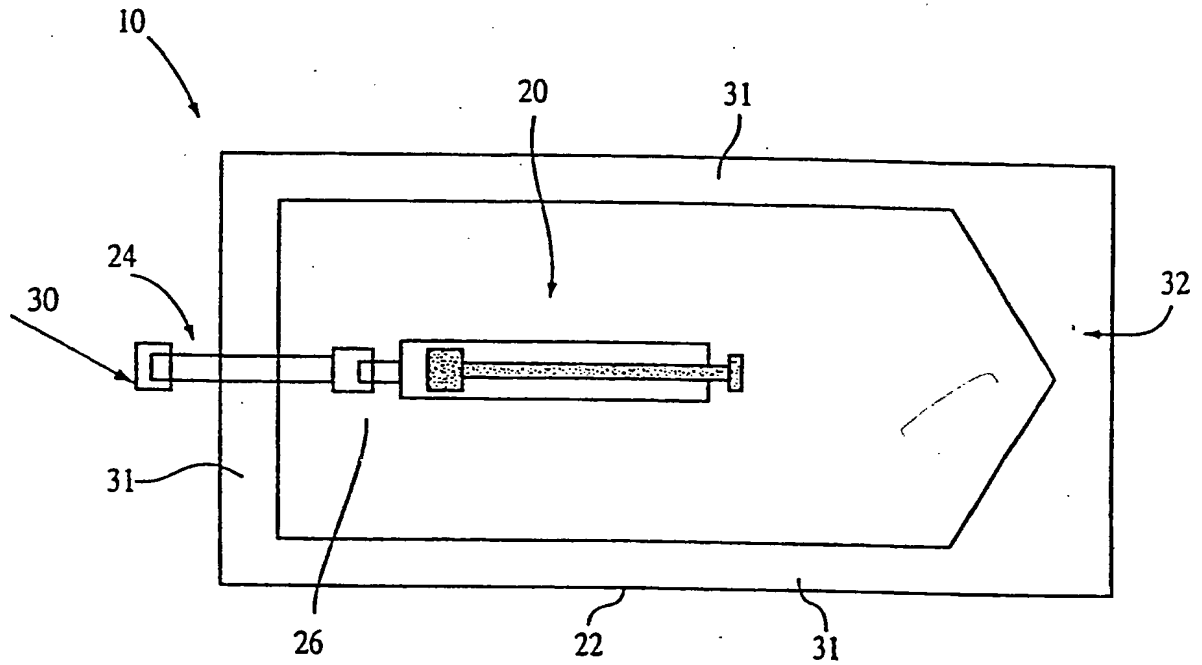


FIG. 1A

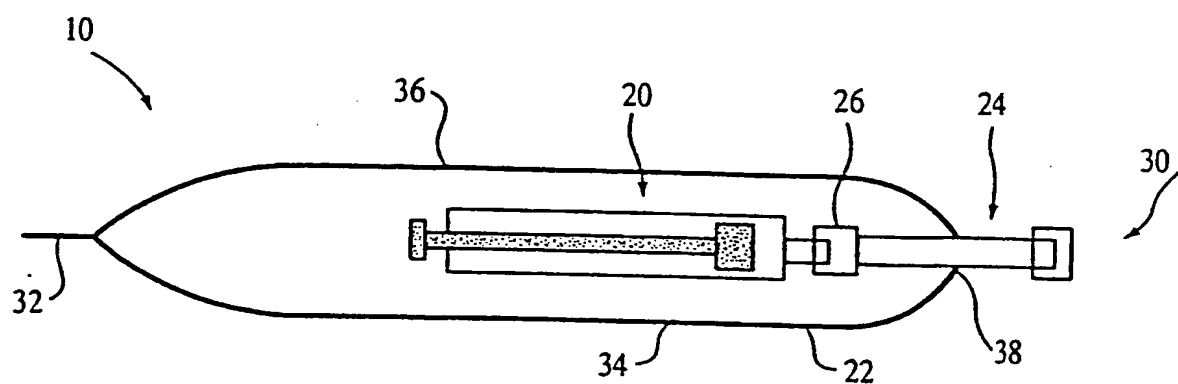


FIG. 1B

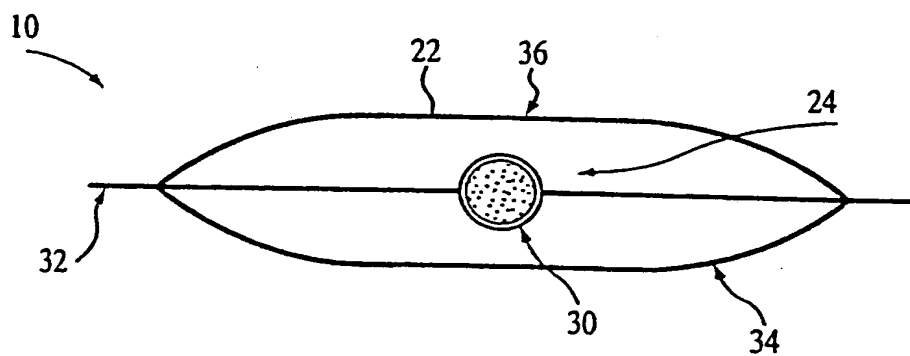


FIG. 1C



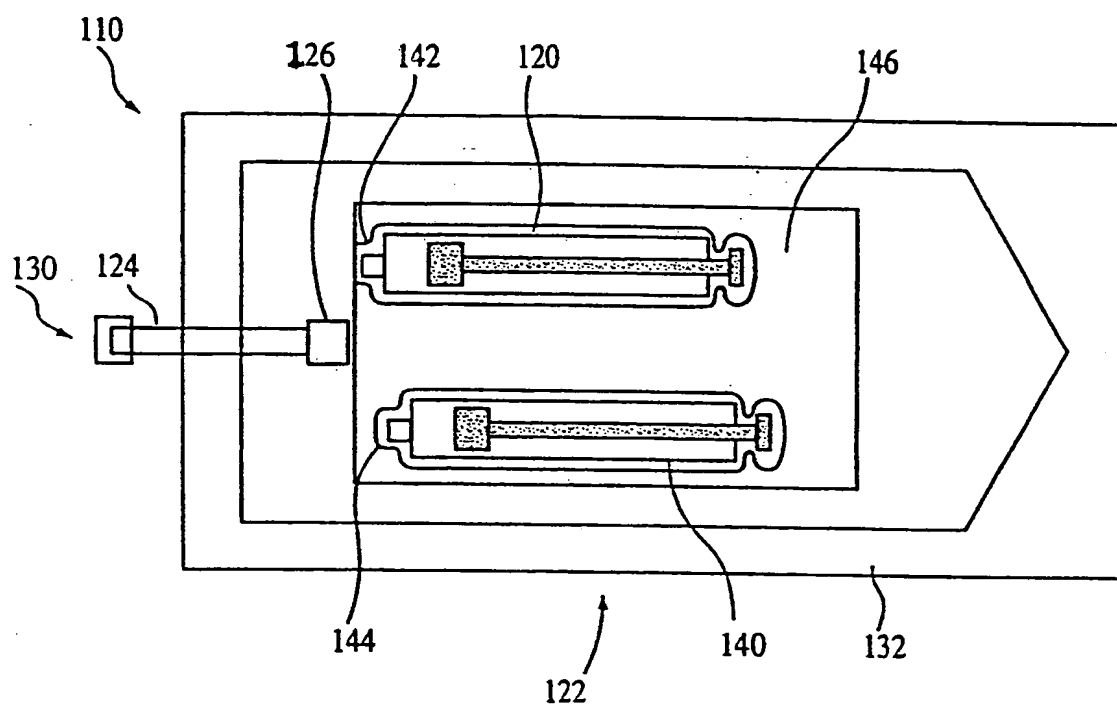


FIG. 2

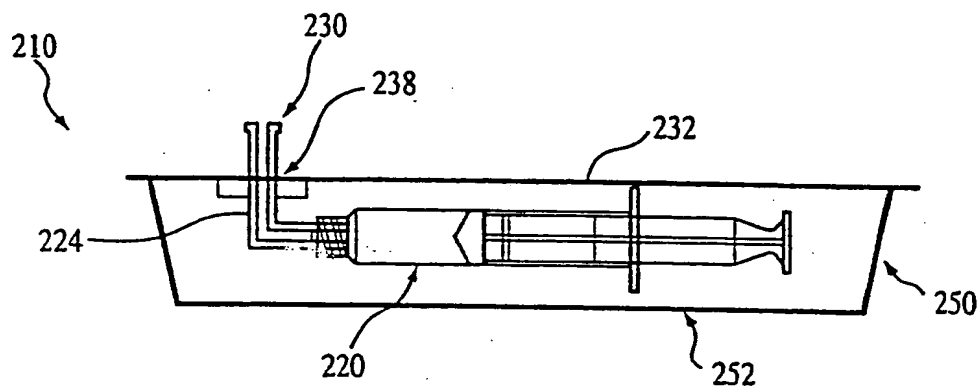


FIG. 3

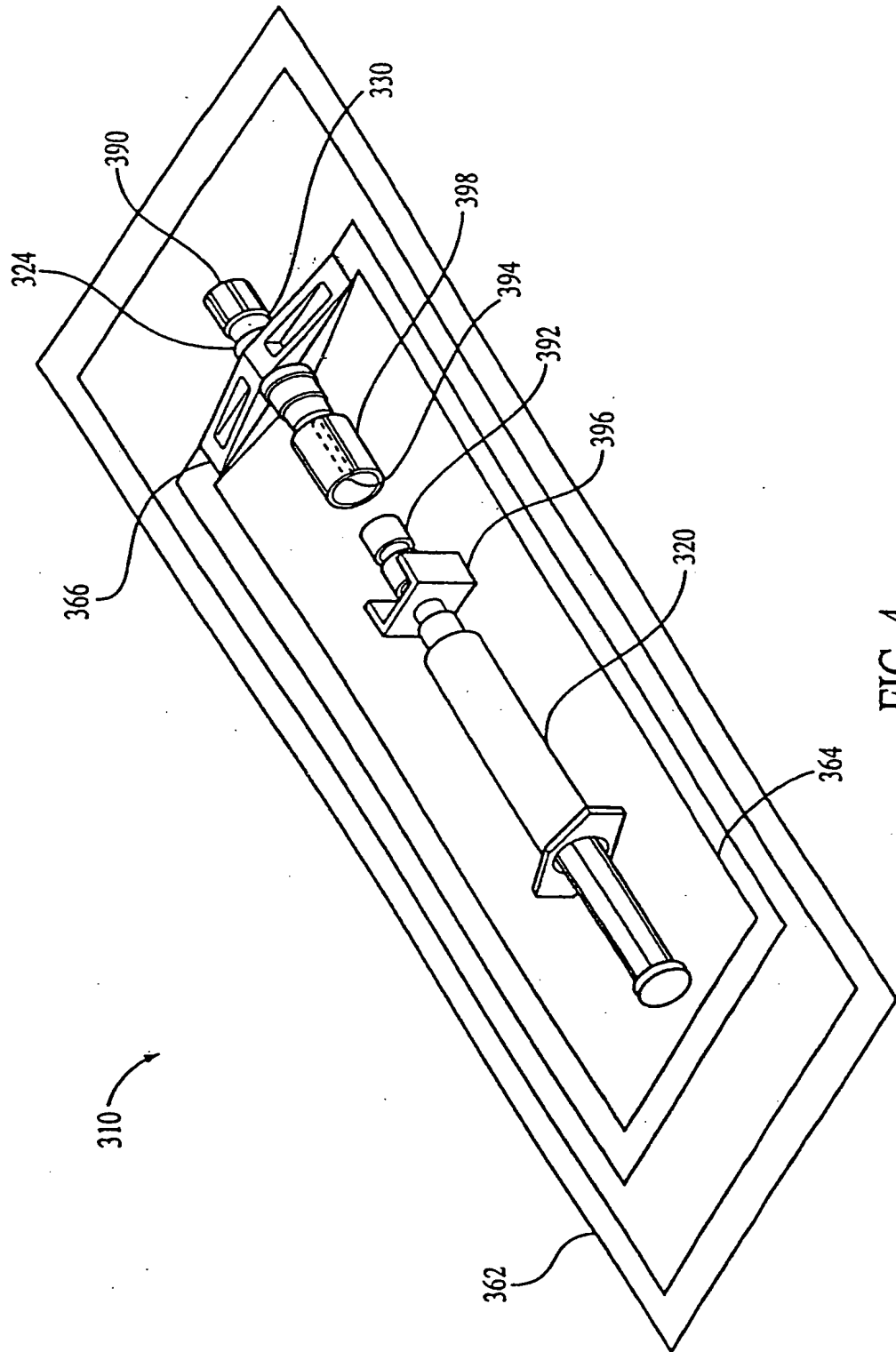


FIG. 4

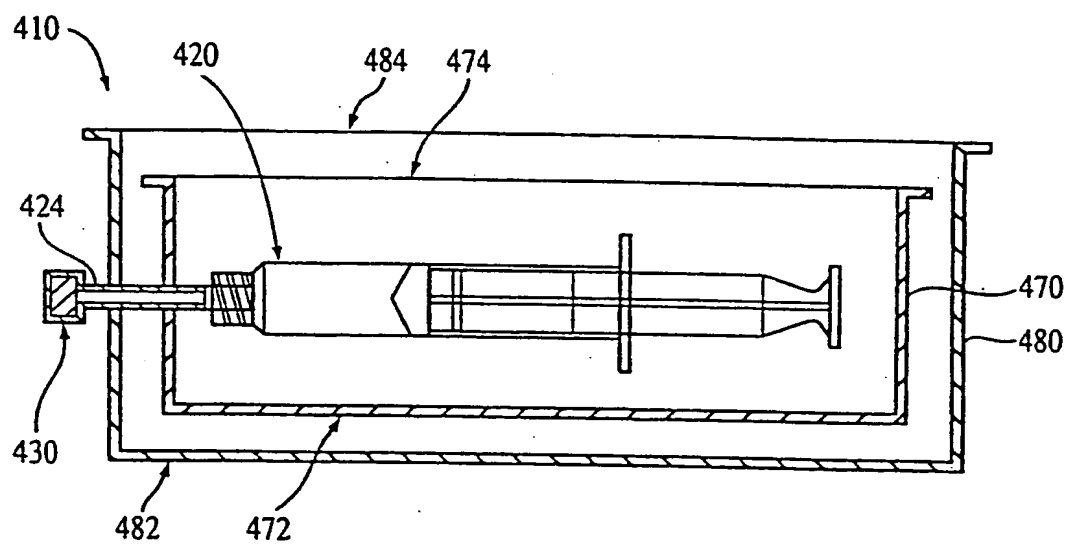


FIG. 5

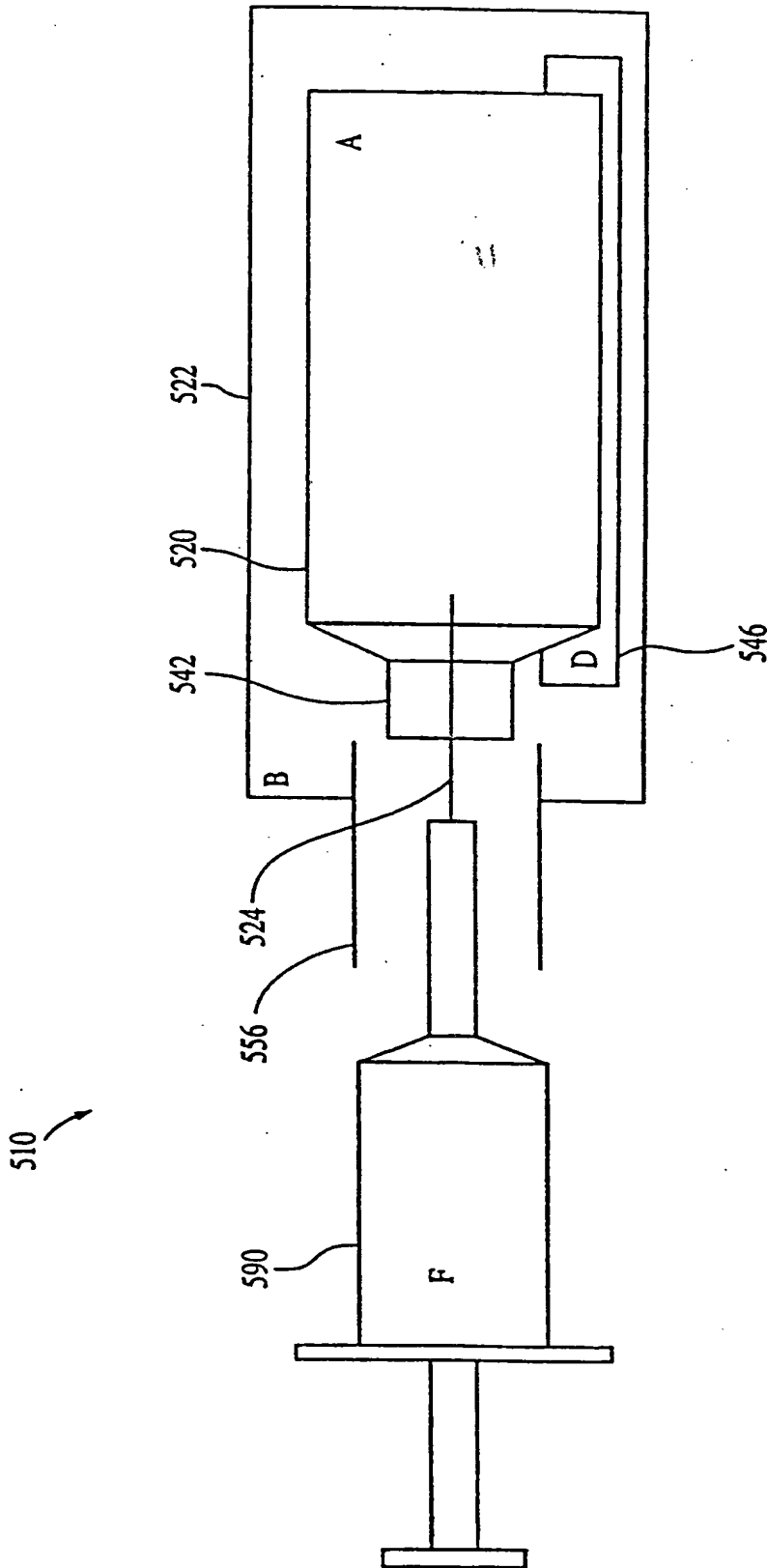


FIG. 6

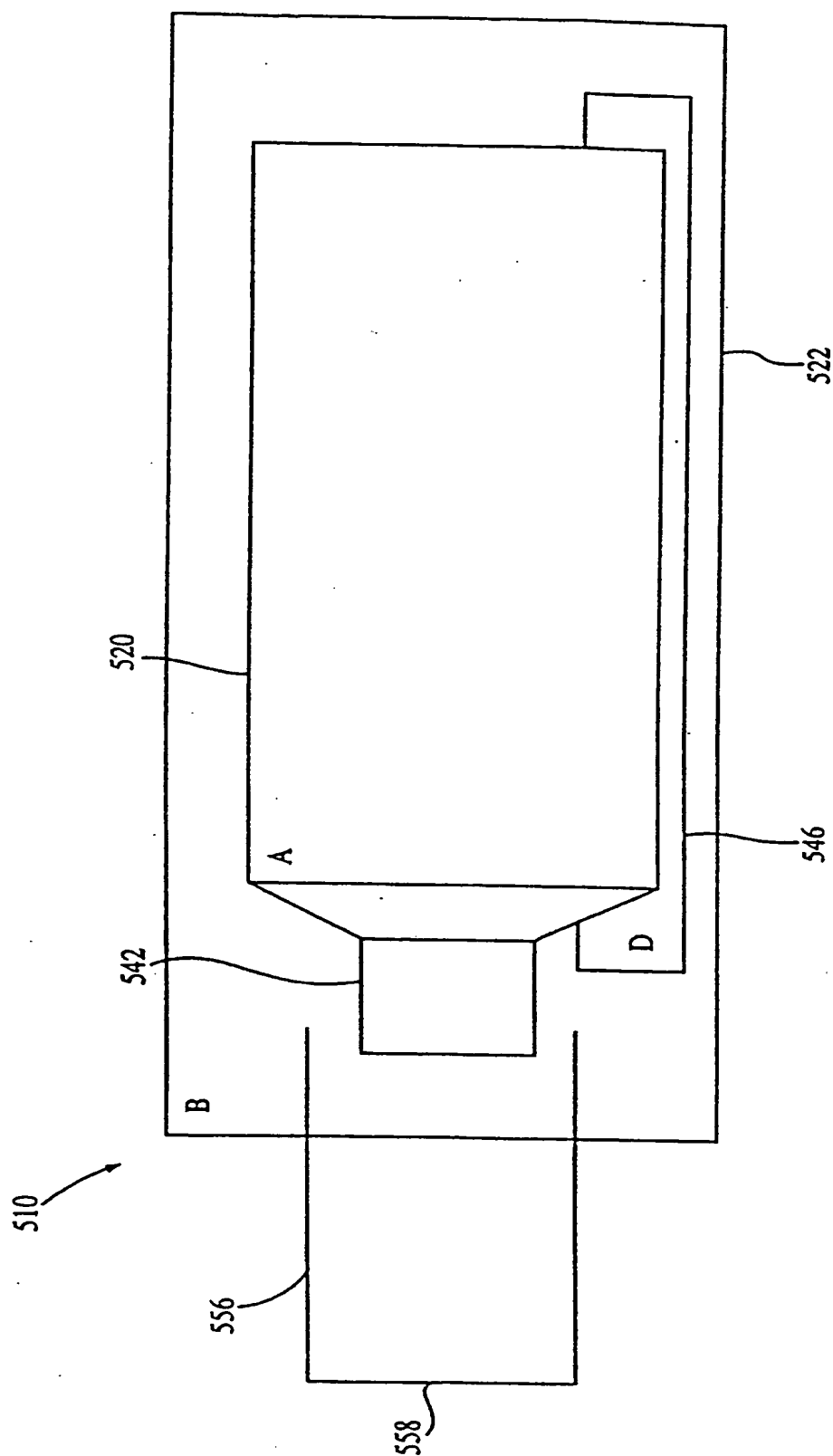


FIG. 7

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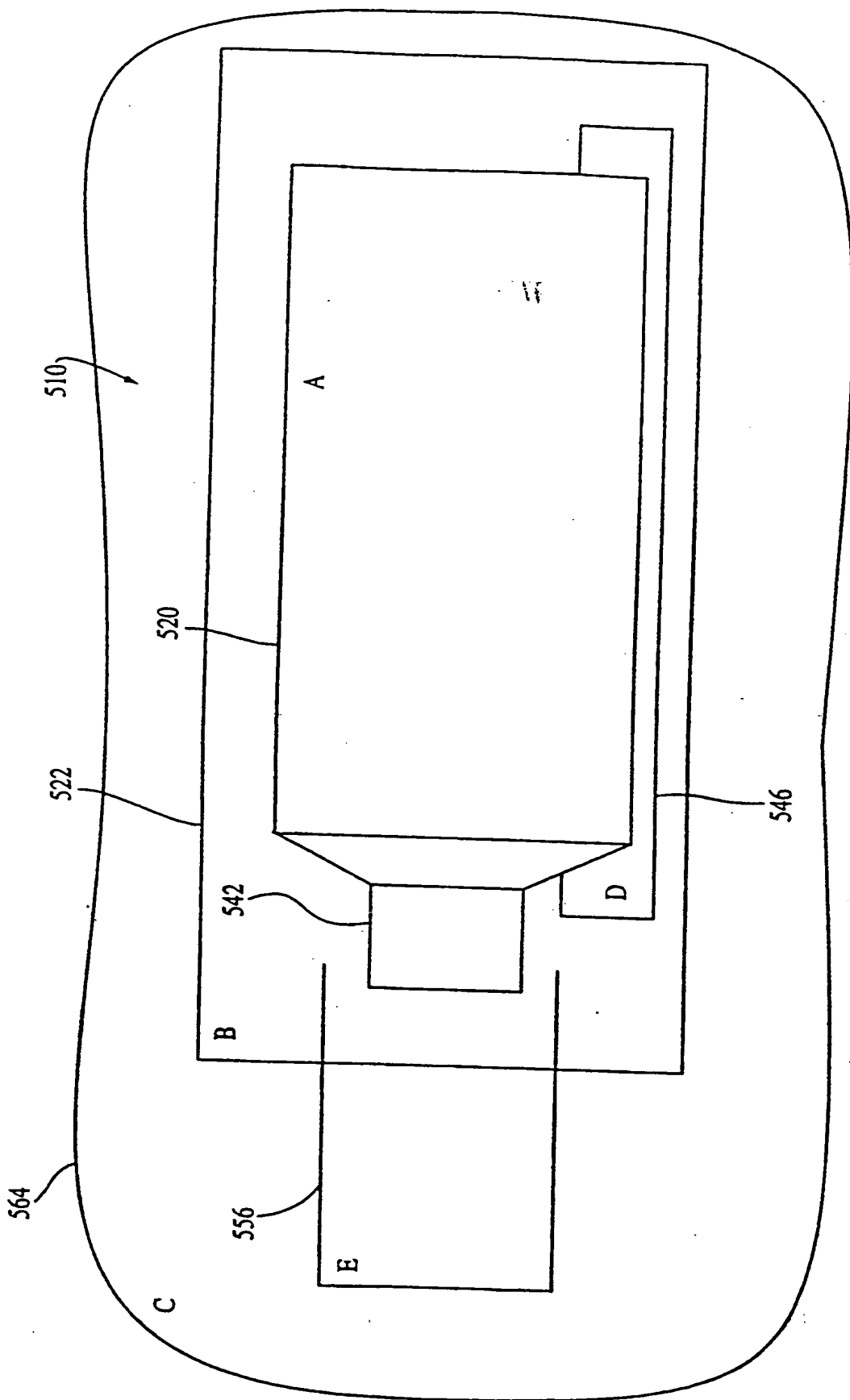


FIG. 8

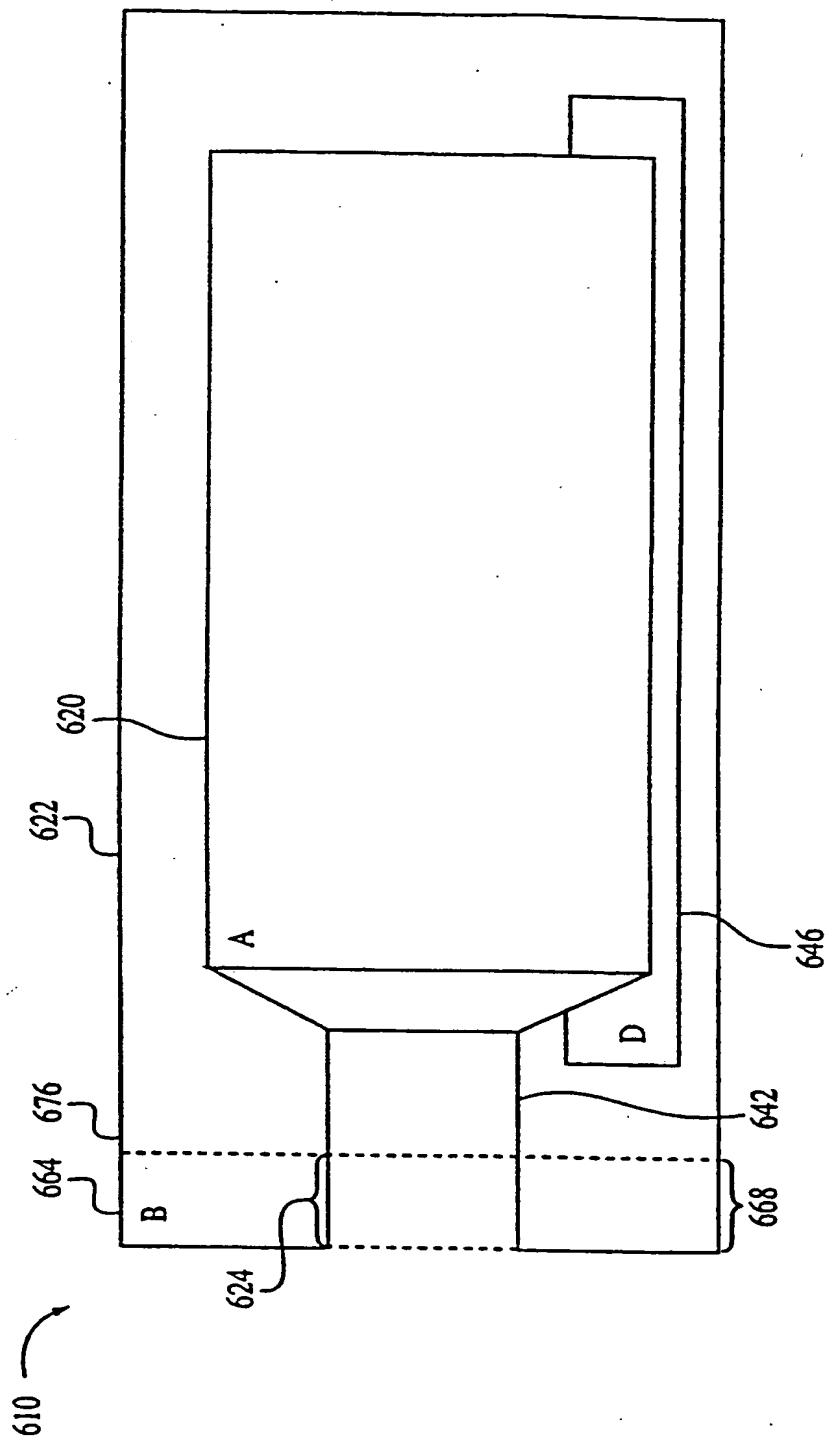


FIG. 9



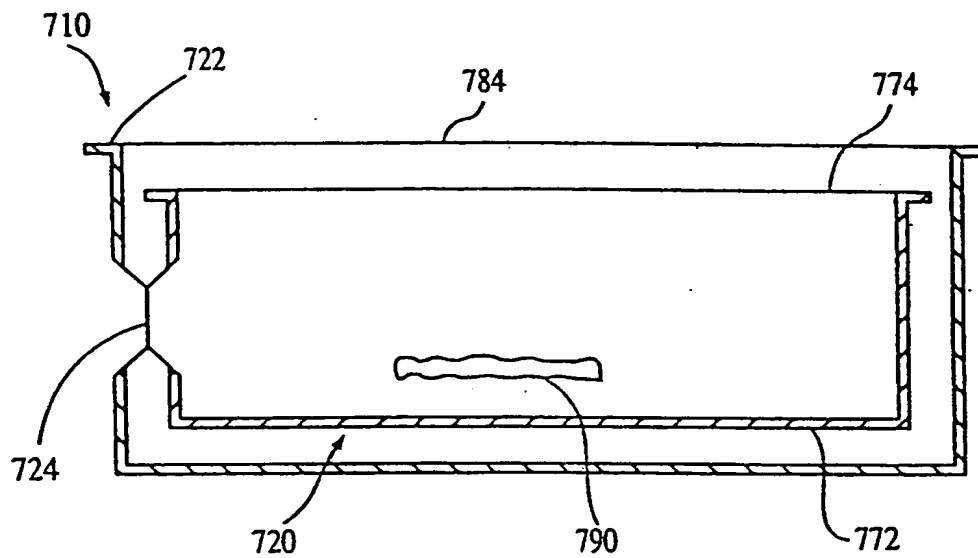


FIG. 10

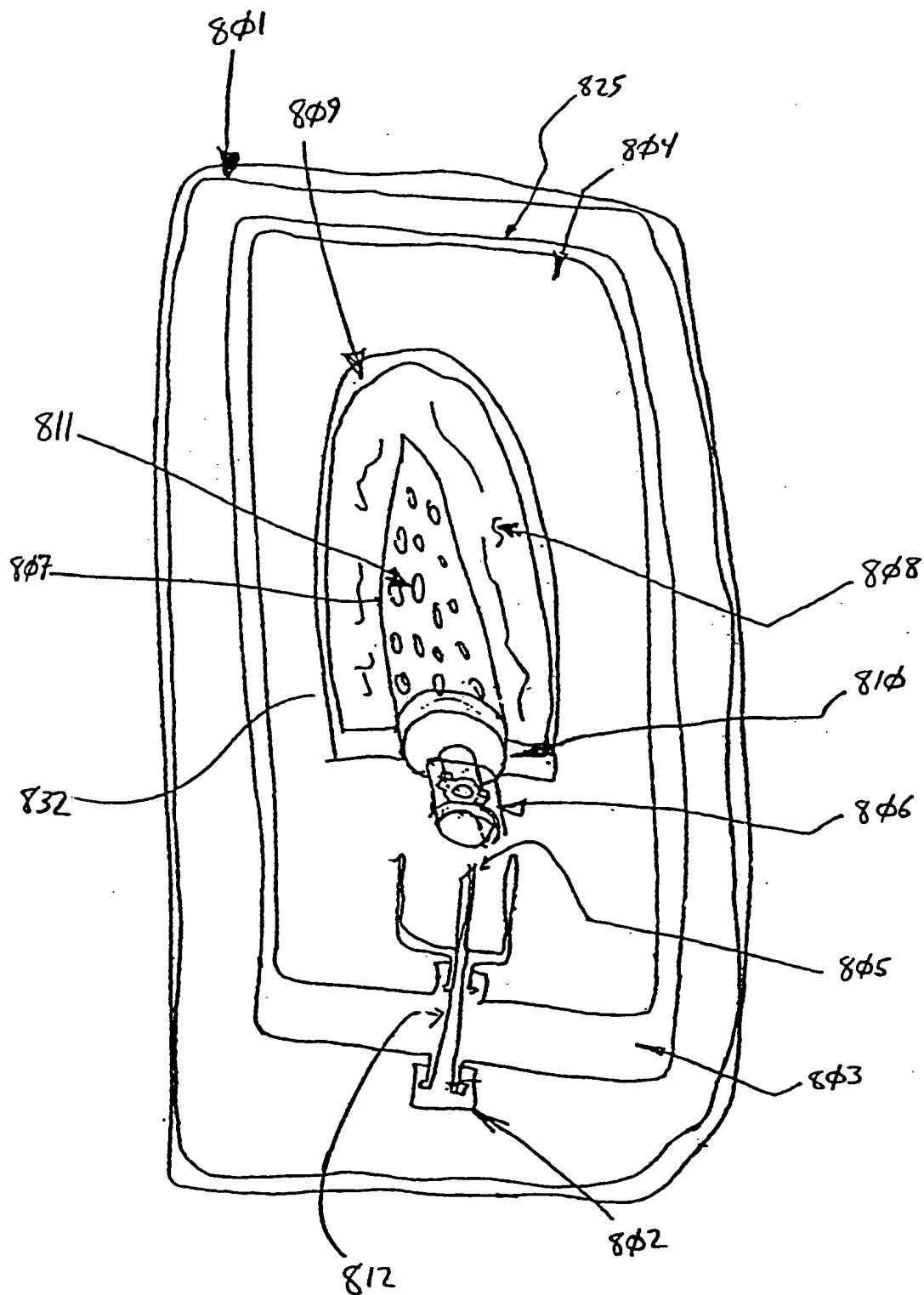
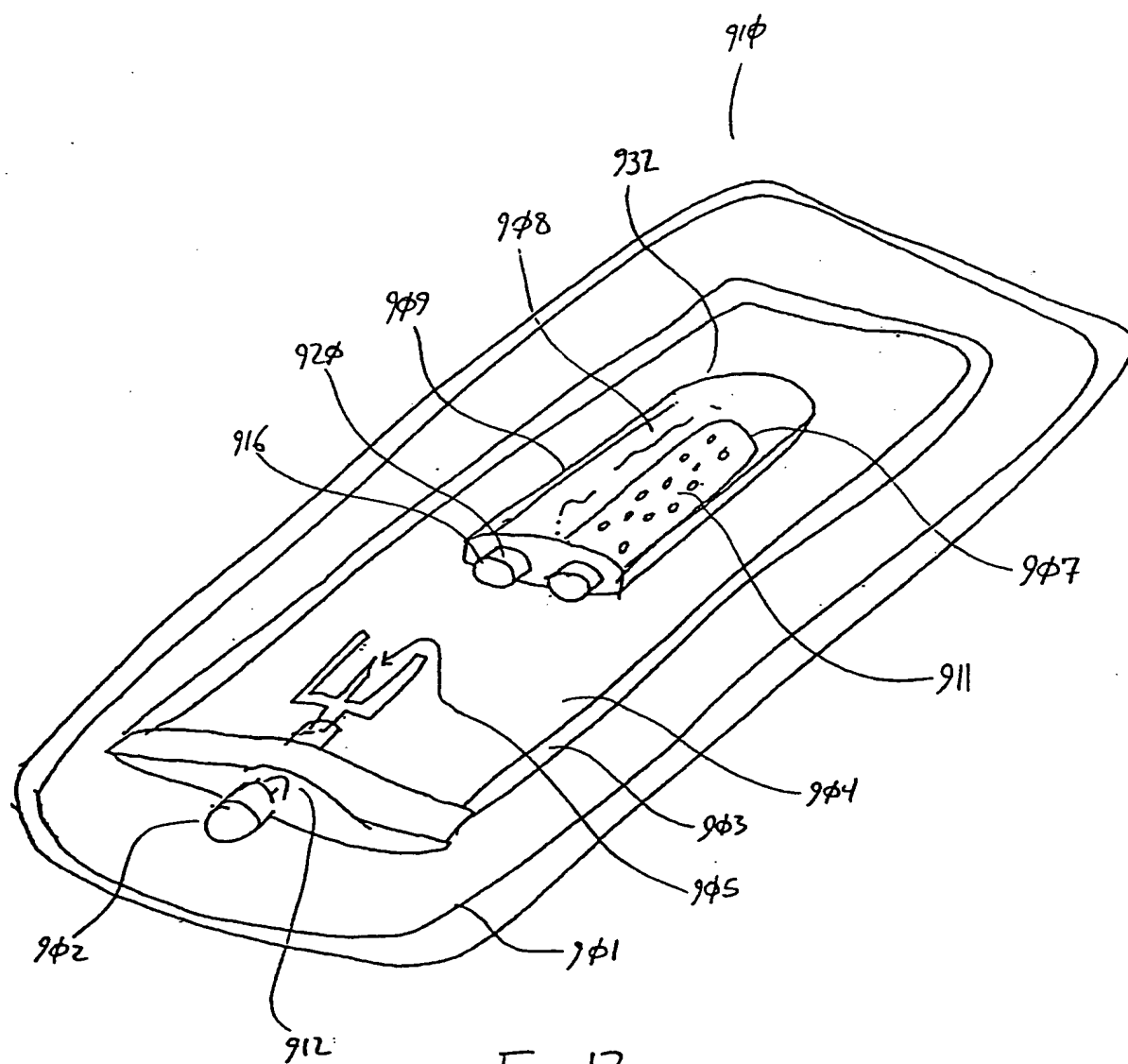


FIG. 11



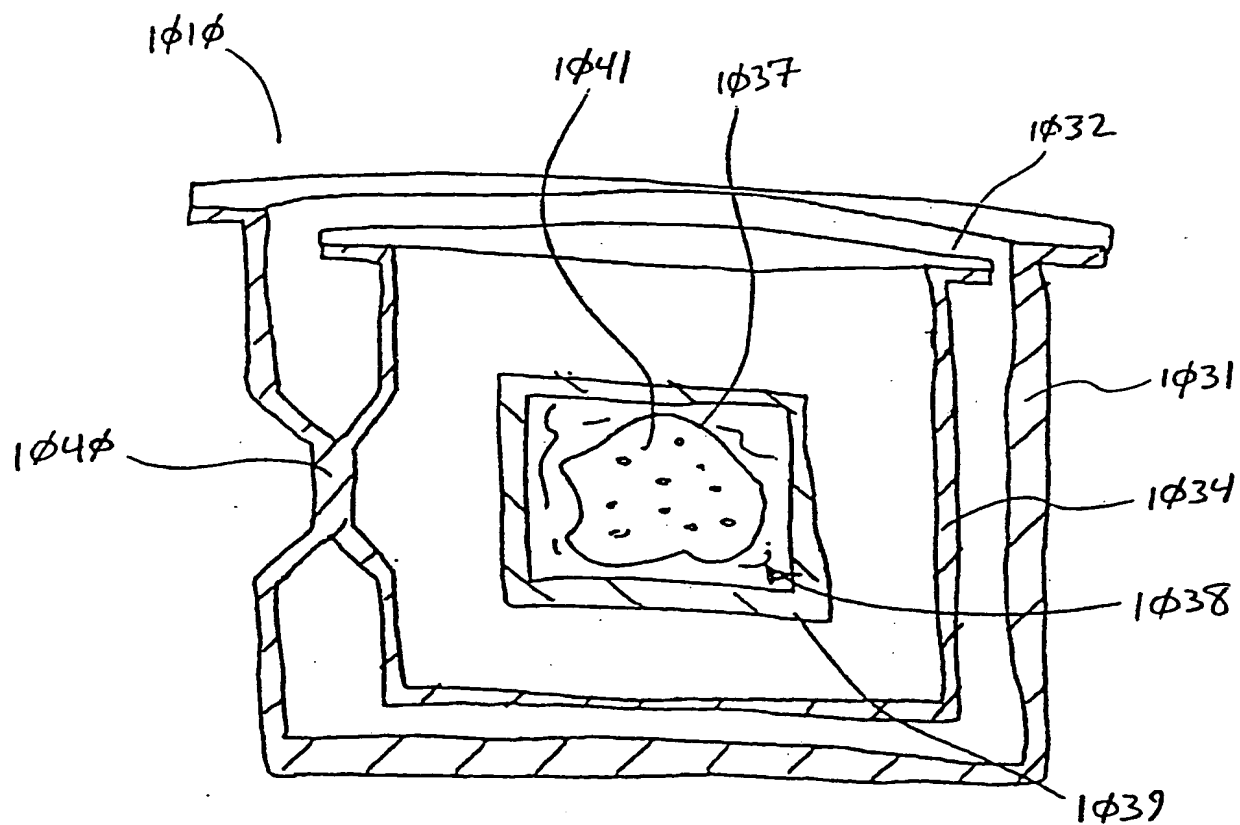


FIG. 13

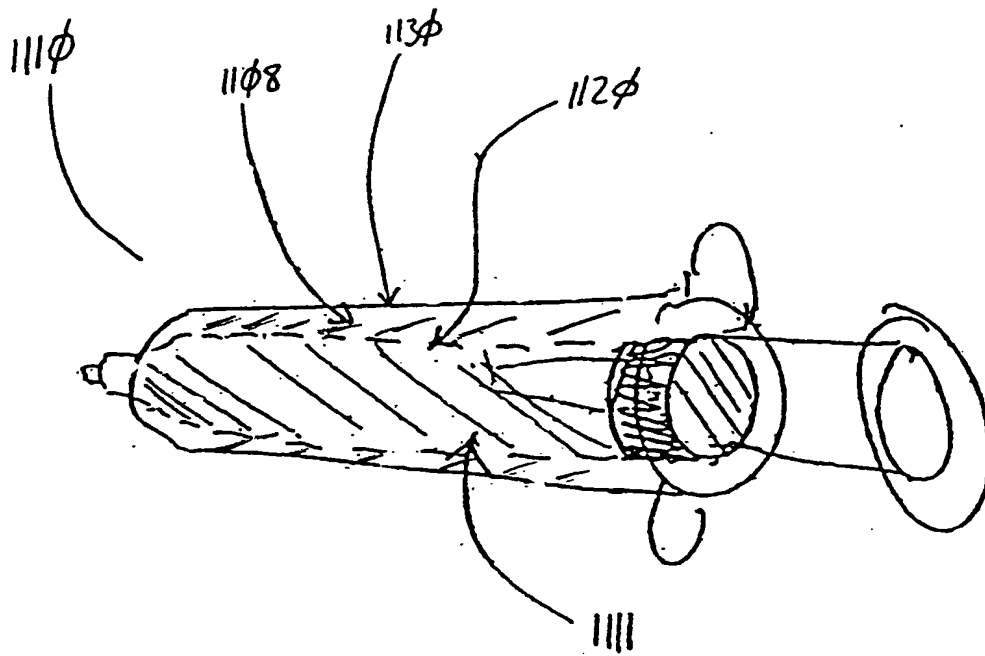


FIG. 14

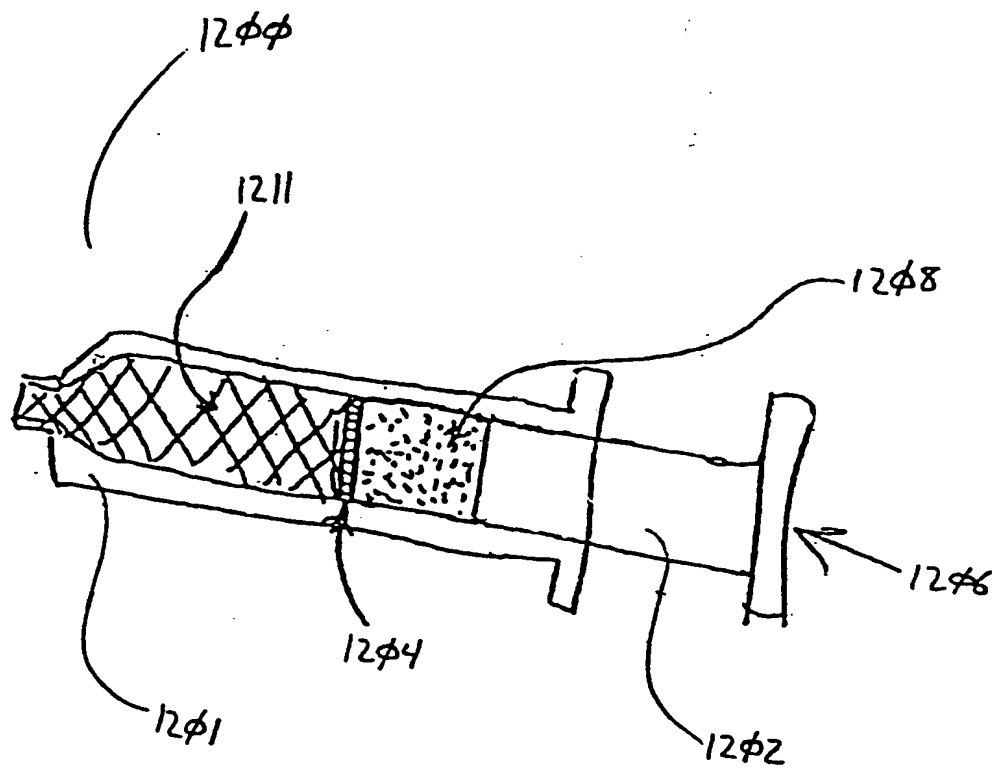


FIG. 15

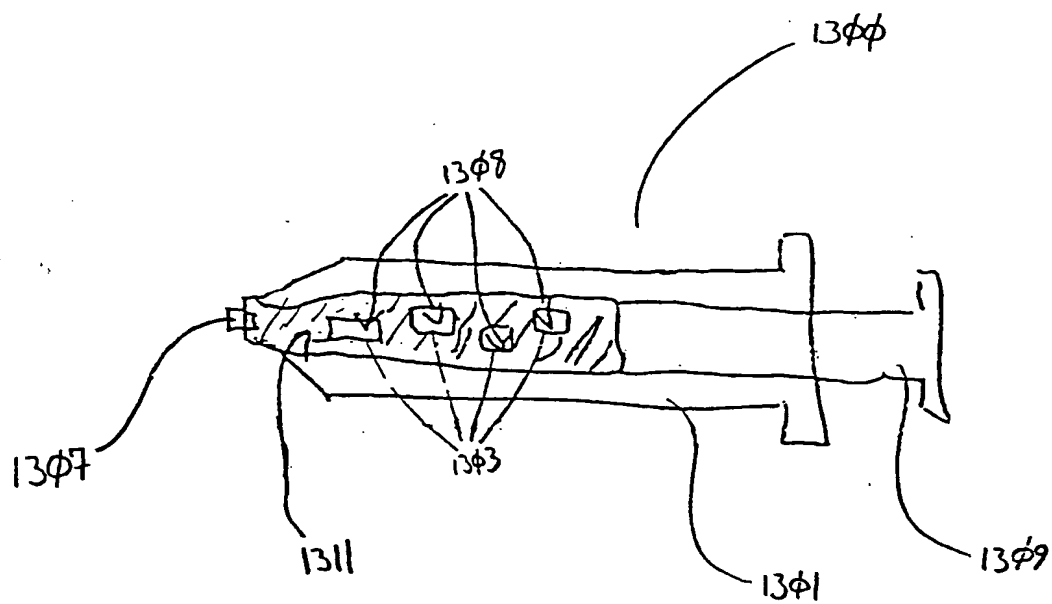


FIG. 16

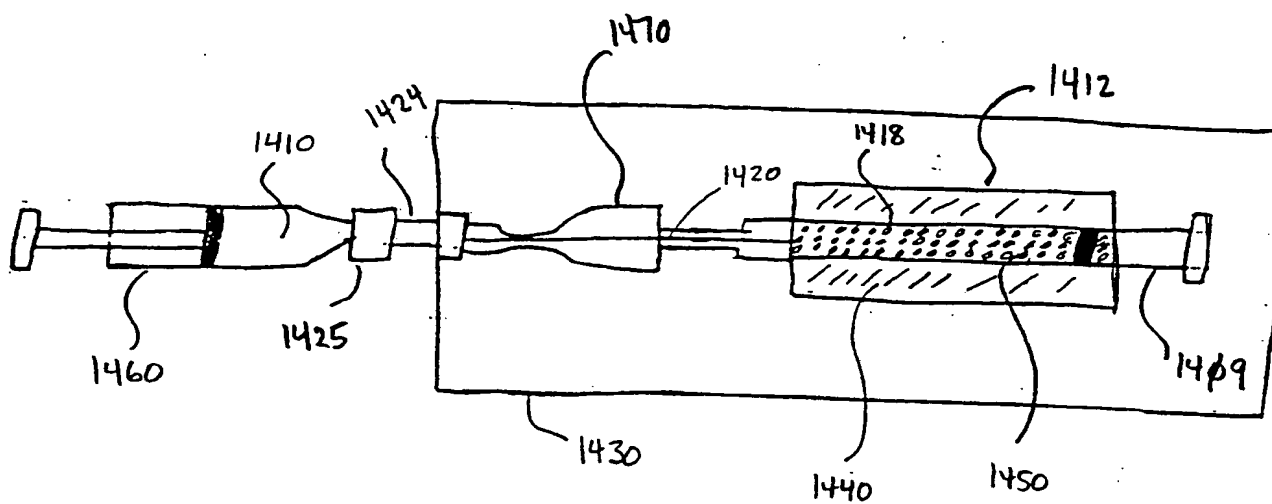


FIG. 17A

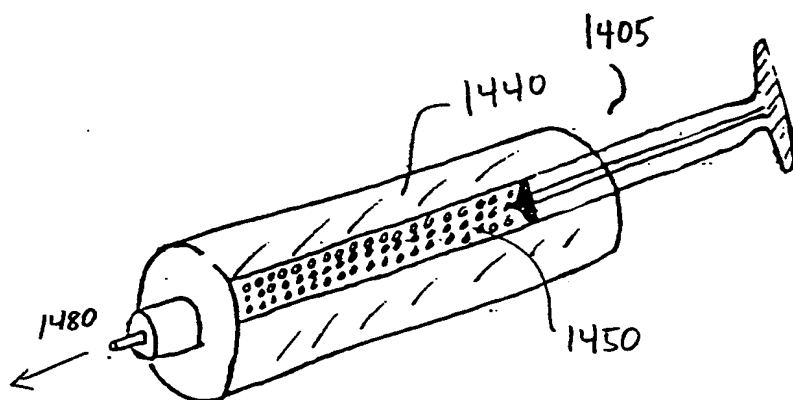


FIG. 17B



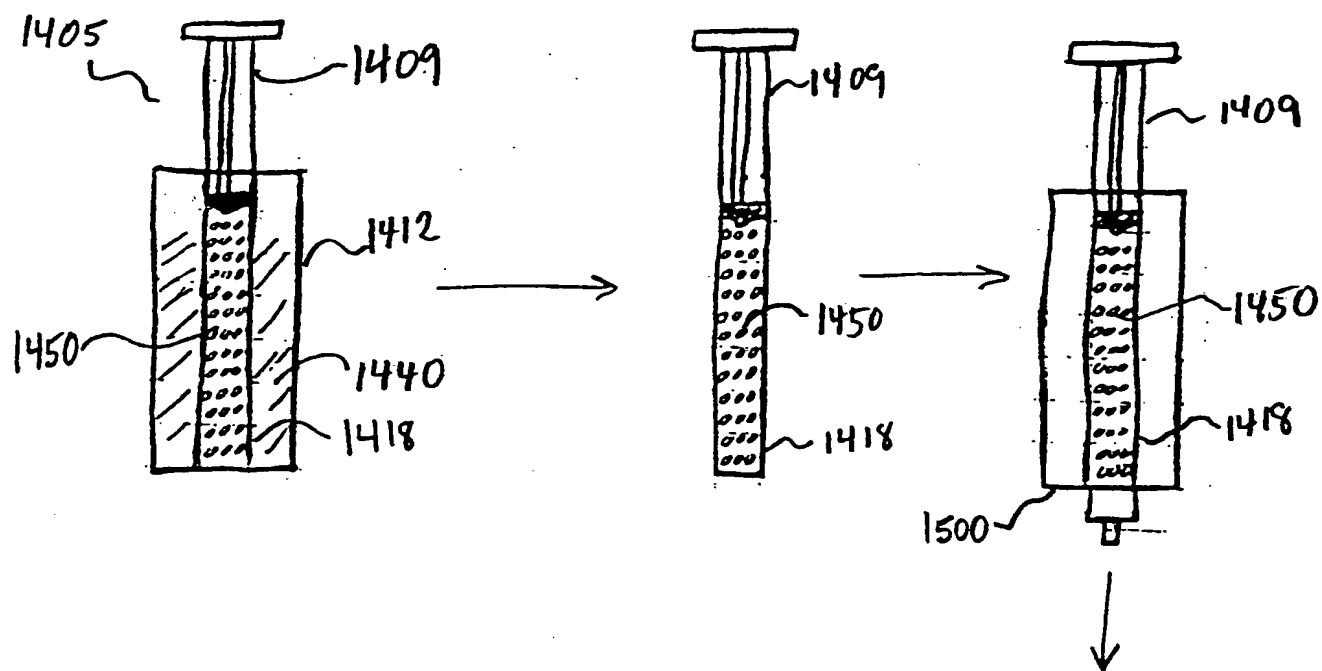


FIG. 18

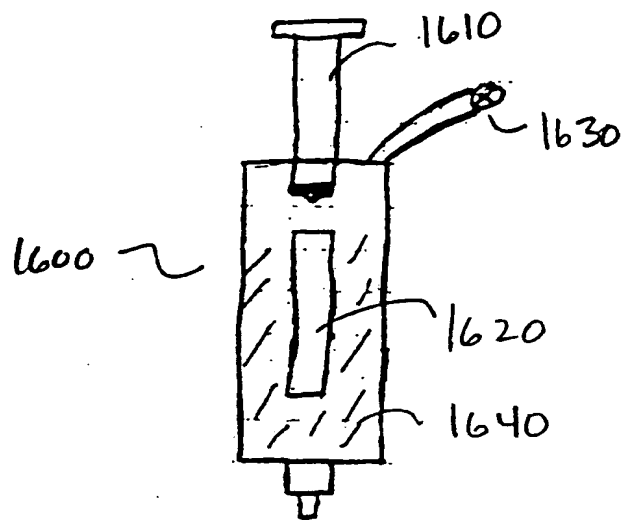


FIG. 19

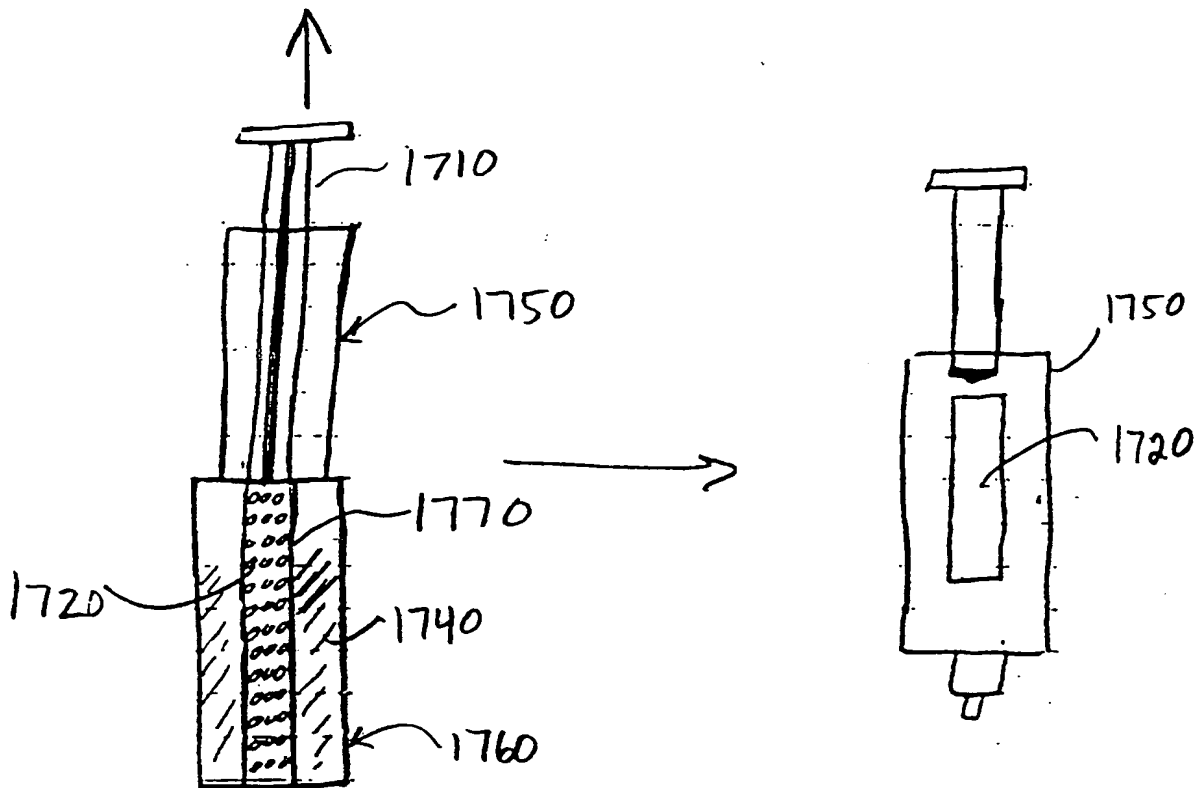


FIG. 20

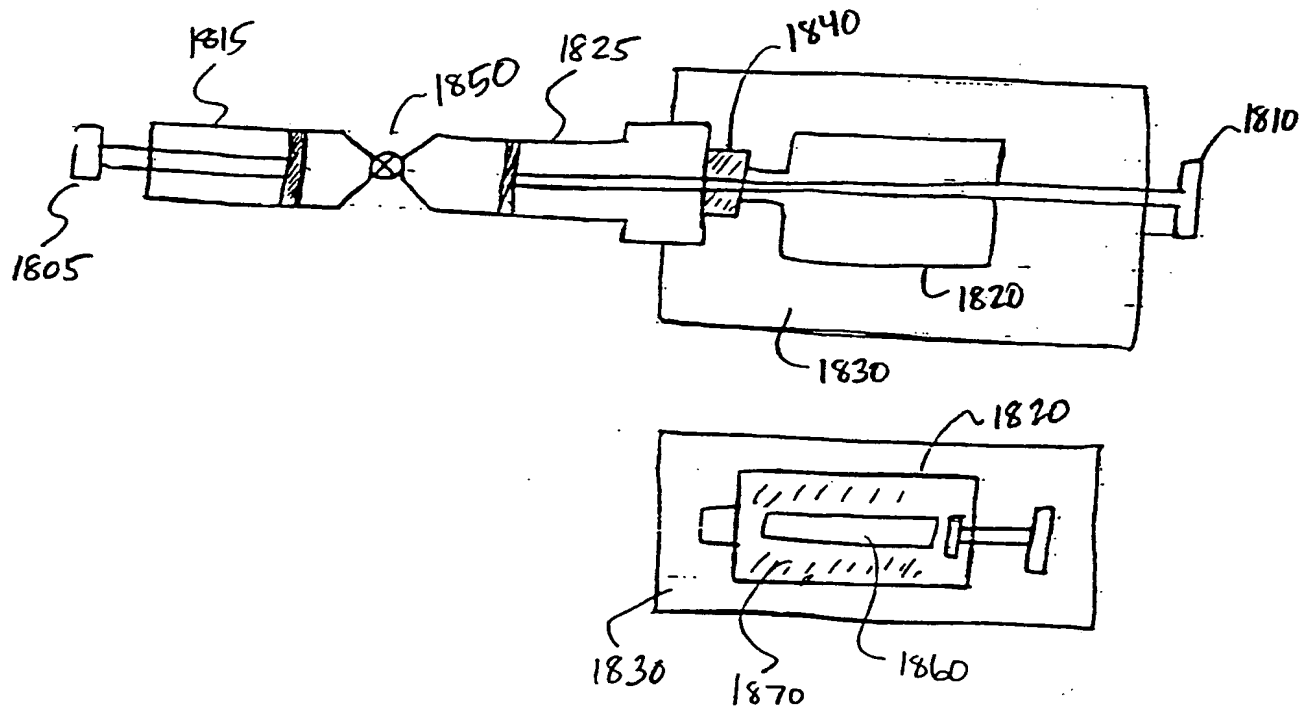


FIG. 21

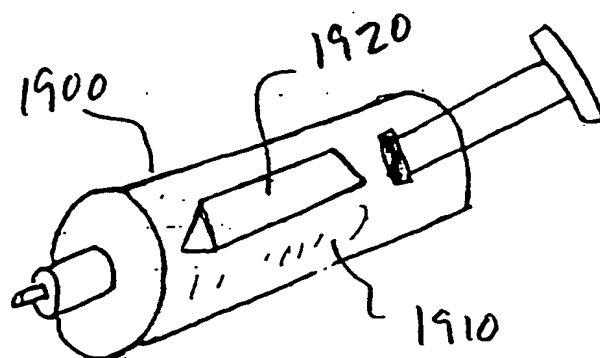


FIG. 22

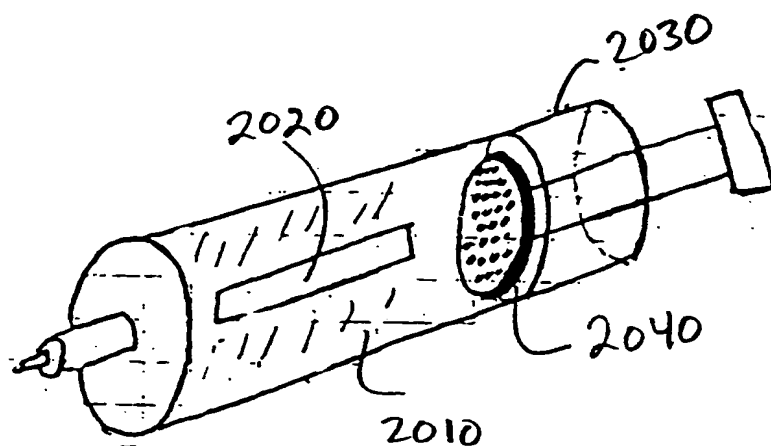


FIG. 23

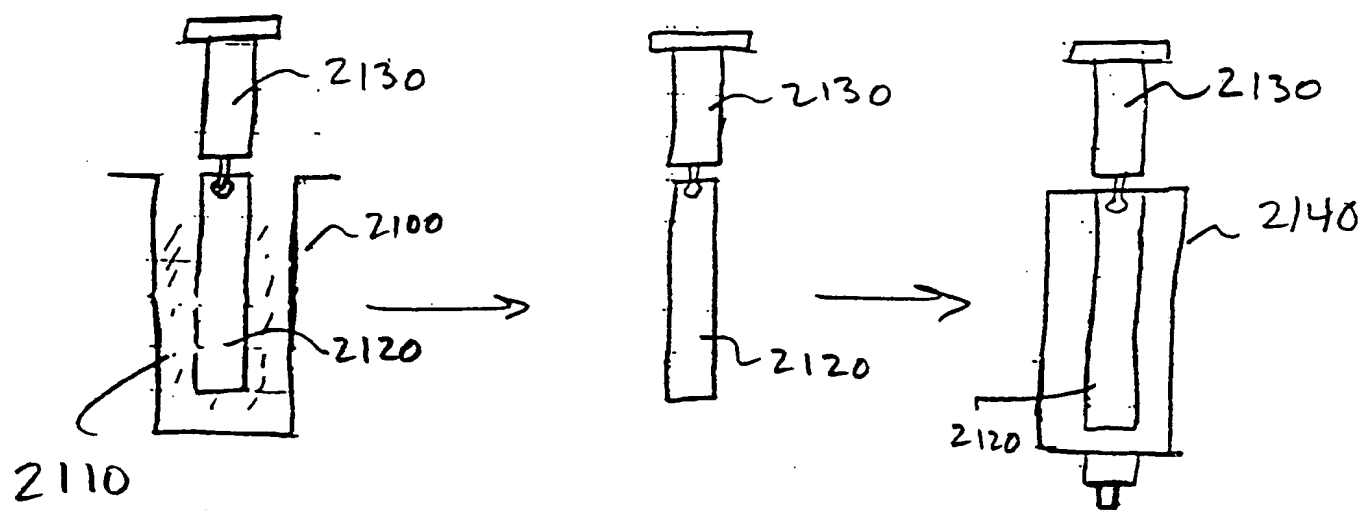


FIG. 24

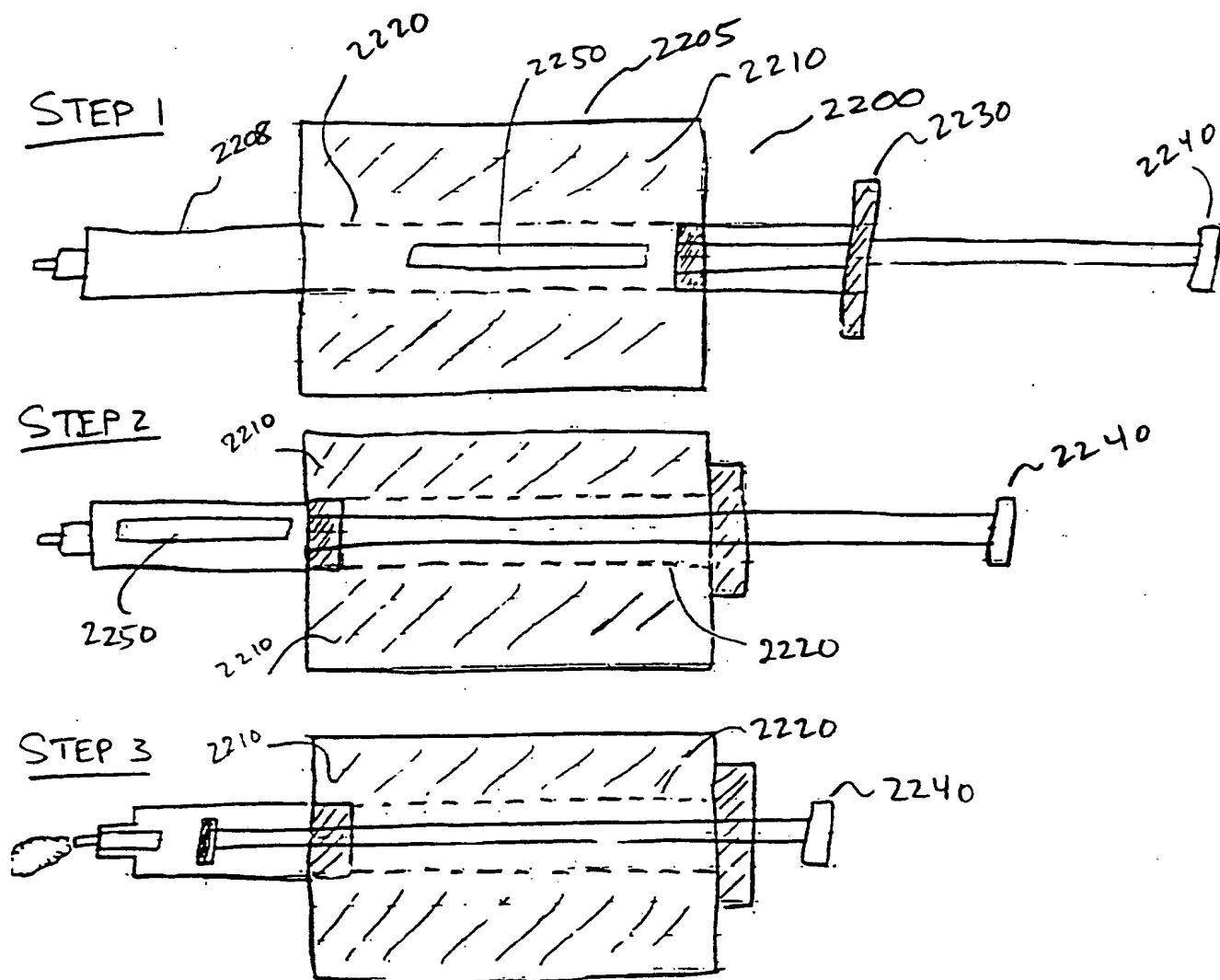


FIG. 25

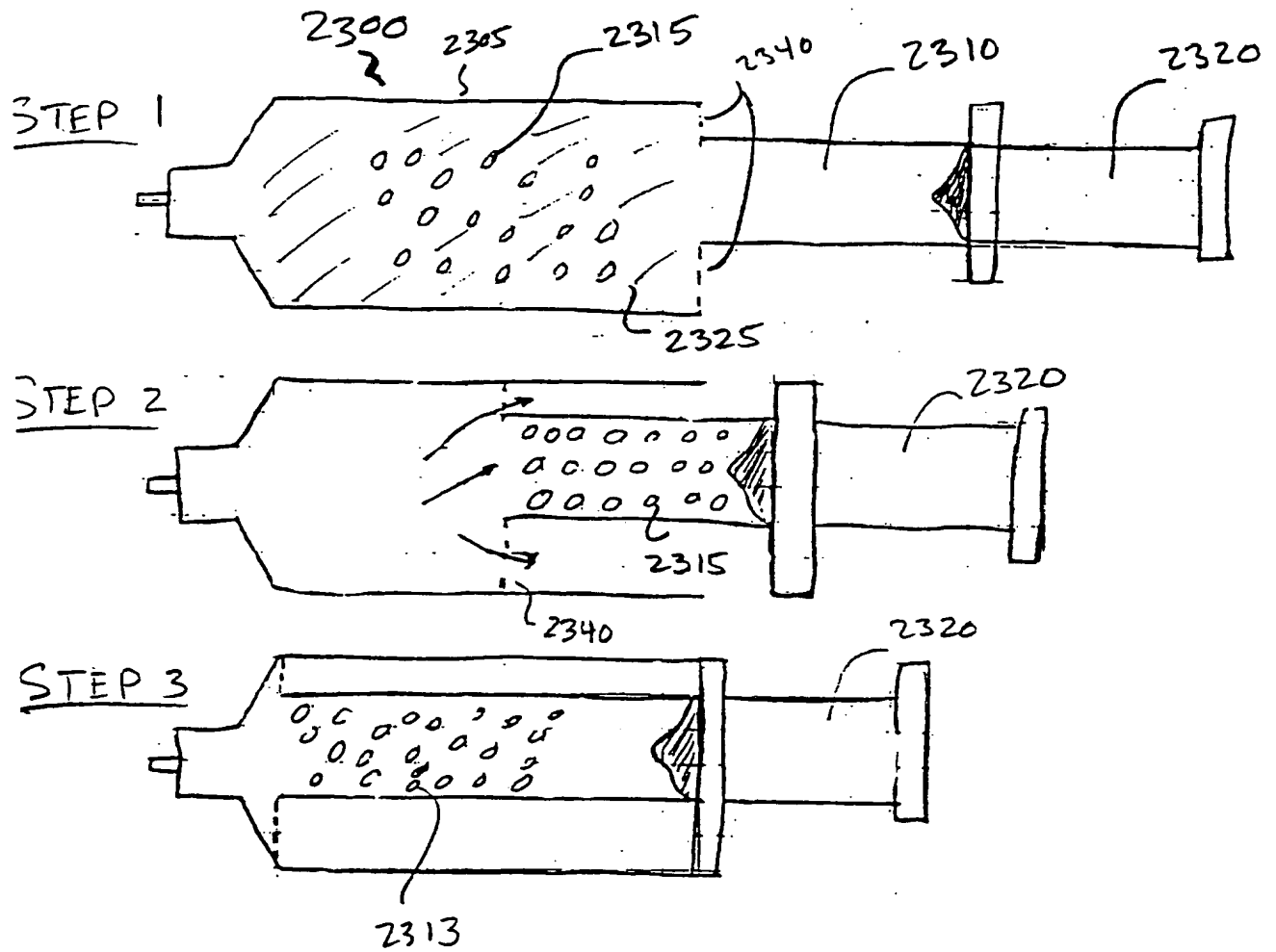


FIG. 26